ETS
ISSUE BINDER

ETS AND
RESPIRATORY
DISEASES & CONDITIONS
IN NON-SMOKING
ADULTS & CHILDREN

I

ETS AND
RESPIRATORY DISEASES AND CONDITIONS
IN NONSMOKING ADULTS AND CHILDREN

VOLUME I

THIS ISSUE BINDER IS INTENDED TO PROVIDE A BASIC,
COMPREHENSIVE REVIEW OF THE SCIENTIFIC LITERATURE
REGARDING A SPECIFIC TOPIC ON ETS AND THE HEALTH OF
NONSMOKERS.

PRIMARY STUDIES AND REVIEWS HAVE BEEN HIGHLIGHTED
TO IDENTIFY (1) USEFUL OR HELPFUL INFORMATION (YELLOW
HIGHLIGHT) AND (2) ADVERSE RESULTS OR OPINIONS (BLUE
HIGHLIGHT).

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INTRODUCTION
ETS AND CHILDHOOD AND ADULT RESPIRATORY DISEASE/SYMPTOMS

This issue binder is designed to provide a comprehensive review of the major literature on environmental tobacco smoke and childhood and adult respiratory disease/symptoms. The book has been divided into subsections: (A) childhood respiratory disease/symptoms; (B) childhood pulmonary function; (C) compromised children such as asthmatics and children with cystic fibrosis; (D) otitis media; (E) adult respiratory disease/symptoms; (F) adult pulmonary function; (G) compromised adults; and (H) confounders.

Each section provides a short introduction to the topic. Major studies are preceded by a short abstract and followed by published critiques of the study. Each of the studies is highlighted to facilitate understanding of the issue: 1) favorable points are highlighted in yellow, and 2) unfavorable points are highlighted in blue. Tables and charts in the notebook are also highlighted in yellow (favorable) and blue (unfavorable).

STUDY ABSTRACTS

In the majority of cases, the abstract or summary that precedes the individual study is the actual quoted abstract of the article's authors. However, some authors did not present an appropriate summary or abstract in their article. In those cases, a brief summary of the article was prepared. The abstracts and summaries prepared by the individual authors of the studies are designated as "abstracts" and "summaries."

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PARENTAL SMOKING AND CHILDHOOD RESPIRATORY DISEASE/SYMPTOMS

PARENTAL SMOKING

Perhaps no claim regarding environmental tobacco smoke (ETS) is as capable of provoking strong feelings as the charge that parents who smoke may compromise the health of their children. While the issue of parental smoking is laden with emotion, the scientific basis for the claim is difficult to interpret. None of the studies that have reported an association between parental smoking and a child's increased risk of developing respiratory infections or symptoms have actually measured exposure to ETS. Virtually all of the studies have failed to control for cross-infections in the home and other important confounding factors. Studies that have controlled for such factors have frequently reported no significant increased risk of respiratory disease in the children of smoking parents.[1-17]

The studies on parental smoking, each with a different sample size, data collection method and analysis, tend to yield factually incompatible and contrary conclusions. For instance, although certain studies and reviews have reported adverse findings,[18-42] others have observed no significant relationship between parental smoking and respiratory illness in children.[5,6,8,43-53] After a five-year study of over 400 children, for example, Dutch researchers concluded there was "no evidence" that parental smoking had an appreciable effect on respiratory symptoms in school children.[49] A similar conclusion was reached by a group of U.S. researchers, including a critic of smoking, who found "no significant relation" between parental smoking and

respiratory symptoms in a study of nearly 400 families with 816 children in three cities.[43]

In 1988, investigators re-examined thirty studies on ETS exposures among children and evaluated the studies for their scientific validity.[54] They noted that while several studies had reported a statistically significant relationship between ETS exposure and respiratory illness in children, "most studies had significant design problems that prevent reliance on their conclusions." The authors concluded that "many questions remain, and future studies should consider important methodological standards to determine more accurately the effect of passive smoking on child health." In 1990, another group of researchers examined the existing literature on ETS and respiratory health.[55] Although critical of ETS, they concluded that "[f]urther studies of health effects are needed; such studies will require improved methods of exposure assessment, as well as better understanding of dose-response relationships."

The studies on parental smoking have relied solely on questionnaires to obtain exposure data.[55] Reliance on questionnaires casts doubt on the findings of these studies for several reasons. First, it has been noted that even "slight changes" in the way the questions were phrased could result "in substantial differences in the type of responses one obtains."[28] Secondly, one study observed that there was a significant difference in the respiratory symptoms reported depending on which

parent completed the questionnaire.[38] It has been reported that mothers are more likely than fathers to report chronic respiratory problems in their children and that asymptomatic mothers are less likely than symptomatic mothers to report symptoms in their children.[55] It has been suggested that "[t]hese potential biases must be evaluated in epidemiologic studies."[55]

In conclusion, although a number of studies have been conducted on parental smoking and childhood respiratory health, the results of these studies are inconsistent and are limited by the methodology employed in each study. Questionnaires are not an accurate method of determining the actual exposure of ETS a child receives from his/her smoking parent. Many studies report no relationship for parental smoking, particularly when confounding factors such as diet, home dampness or cross-infection in and outside the home are considered. Childhood respiratory illness appears to be influenced by many different social, familial, and environmental factors. To isolate parental smoking as a cause is scientifically unjustified.

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ABSTRACT: This study replicated and extended earlier research that indicated a greater prevalence of respiratory illness among children subjected to tobacco smoke in the home environment. A random phone sample of 2,626 households in Detroit, Long Beach, and Pasadena, yielded evidence that (a) children subjected to tobacco smoke in the home environment have a greater prevalence of acute illness when compared to children in smoke-free environments, (b) adult nonsmokers subjected to tobacco smoke in the home environment may have a greater prevalence to acute illness than adult nonsmokers who reside in a smoke-free environment, and (c) respiratory illness rates may be related to air pollution rates in metropolitan areas.

EFFECT OF HOME ENVIRONMENT TOBACCO SMOKE ON FAMILY HEALTH

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This study replicated and extended earlier research that indicated a greater prevalence of respiratory illness among children subjected to tobacco smoke in the home environment. A random phone sample of 2,626 households in Detroit, Long Beach, and Pasadena, yielded evidence that (a) children subjected to tobacco smoke in the home environment have a greater prevalence of acute illness when compared to children in smoke-free environments, (b) adult nonsmokers subjected to tobacco smoke in the home environment may have a greater prevalence of acute illness than adult nonsmokers who reside in a smoke-free environment, and (c) respiratory illness rates may be related to air pollution rates in metropolitan areas.

This article reports a further study of the relationship of tobacco smoke in the home to the prevalence of illness in children. It represents an attempt to replicate the earlier finding that there is a greater prevalence of acute illness in children subjected to tobacco smoke in the home environment than for those children not subjected to tobacco smoke in the home environment (Cameron, 1967; Cameron, Kostin, Zaks, Wolfe, Tighe, Oselett, Stocker, & Winton, 1969). Only two areas of the country, Denver and Detroit, have been sampled in previous studies; this study samples Detroit, Long Beach, and Pasadena.

METHOD

As it seems tentatively established that there is a reasonable degree of communality between random phone sampling and random area sampling in the establishing of acute illness rates (Cameron et al., 1969), we randomly drew 2,150 phone numbers from the Detroit metropolitan, 363 numbers from the Long Beach, and 161 from the Pasadena phone books (a larger number from both Long Beach and Pasadena had been planned but various difficulties aborted the samples). Each number was called and households with children under the age of 17 in residence were sampled via the report of an adult member. As we were mainly interested in testing the hypothesis that children residing in home environments with tobacco smoke present suffer a greater prevalence of acute illness, the cutoff age of 16 was employed for comparability with Public Health Service (PHS) surveys. If a business or an inappropriate household (i.e., no children under age 17 in residence) was called, the next phone number

down the column was substituted. All appropriate families who refused an interview were called back to a maximum of 7 times at which point they were considered a refusal. In Detroit, there were 20 refusals (<1%), in Long Beach, there were 8 refusals (2.2%), and in Pasadena, there were 20 (8%). Any drawn phone number that did not answer was called back on 3 different days to establish the number as "dead" for sampling purposes. Interviewers were college student volunteers who had been trained in the administration of the questionnaire. Twenty-five percent of the data was verified by the recalling and readministration of parts of the questionnaire by junior investigators.[2] All sampling took place from November 3 to November 25, 1968.

After an introduction in which the interviewer identified himself as a representative of the National Health Survey, he asked questions concerning demographic variables, family health, smoking habits, ventilation and pollution. A major difference between our and the PHS acute illness questionnaire is that our procedure required the respondents to report on the health of the family for the past 7 days, instead of the past 14 days as required by PHS.

Coding was always done in the same order as the questions were asked so that the coder did not know whether he was coding a person subjected to smoke or not before he coded them ill or not ill. Further, only about 1% of the responses required any interpretive coding—the categories used by the PHS correspond with those used by the general populace (i.e., if the interviewee characterized an illness as a "cold," it was coded as a "cold"; if the illness was said to be the "flu," and vomiting occurred a great deal, it was coded as "influenza with digestive manifestations"—all interpretive codings are in the "other" illness categories).

HYPOTHESIS TESTING EXPLANATION

Before reporting our results, we should probably note that we did not test a non-directional hypothesis with the chi-square statistic. Rather, all chi-squares were derived by testing the specific hypothesis, "Is the respiratory illness prevalence for children subjected to tobacco smoke in the home environment greater than that for children not subjected to tobacco smoke in the home environment?" We felt that the consistency of our previously reported results on this question made testing the null hypothesis of no difference between the two samples a procedure wasteful of information. Therefore, we used the empirically uncovered rate of illness for non-smoke-subjected children in each age grouping to generate the expected prevalence for the smoke-subjected children (e.g., if at a given age category, the non-smoke children had a prevalence of 5%, the chi-square was performed between the expected prevalence at 5% versus the actually obtained figure with $df = 1$). Since the null hypothesis can be rejected because sample "a" is *either* too great or too small relative to sample "b", the greater efficiency of a specific hypothesis, which eliminates essentially half of the non-directional hypothesis, is obvious.

RESULTS

Turning first to the question of whether children subjected to tobacco smoke in the environment have a greater prevalence of respiratory illness than children not subjected, our results rather firmly suggest an affirmative answer. Table 1 summarizes the acute illness rate from each of the three locations. All differences that reach statistical significance are in the affirmative direction. Since the Long Beach and Pasadena samples are rather small to detect reliably a difference for an effect on illness prevalences, the spottiness of results is to be expected. Of additional interest, the prevalence of respiratory illness for children who themselves smoke in each location is greater than that of children who are merely subjected to "second-hand" smoke (7.8% for Detroit, 15.4% for Long Beach, and 28.6% for Pasadena smokers).

Chronic illness prevalences for children subjected to smoke were much the same as those of children not subjected (in Detroit, for example, for 16-year-olds and under, the prevalences were 1.8% and 1.9% with the lower prevalence favoring the smoke-subjected children).

TABLE 1

THE HEALTH OF CHILDREN SUBJECTED TO TOBACCO SMOKE IN THE HOME VERSUS THE HEALTH OF CHILDREN NOT SO SUBJECTED

Age	No. subjected	No. not subjected	x^2
Detroit			
10–16	1,506 (17 smokers)	735	
Respiratory illness	104 (6.9%)	35 (4.8%)	11.45***
Acute illness excluding injuries	143 (9.5%)	49 (6.2%)	
6–9	798	356	
Respiratory illness	83 (10.4%)	30 (8.4%)	3.78**
Acute illness excluding injuries	105 (13.2%)	41 (11.5%)	
0–5	933	423	
Respiratory illness	159 (17.1%)	53 (12.6%)	32.0***
Acute illness excluding injuries	195 (20.9%)	64 (15.1%)	
Long Beach			
10–16	189 (13 smokers)	109	
Respiratory illness	12 (6.3%)	10 (9.2%)	–2.55*
Acute illness excluding injuries	27 (14.3%)	11 (10.1%)	
6–9	110	58	
Respiratory illness	7 (6.4%)	1 (1.7%)	9.03***
Acute illness excluding injuries	8 (7.3%)	4 (6.9%)	
0–5	152	87	
Respiratory illness	20 (13.2%)	9 (10.3%)	–1.03 (ns)
Acute illness excluding injuries	22 (14.5%)	13 (14.9%)	
Pasadena			
10–16	78 (7 smokers)	65	
Respiratory illness	15 (19.3%)	5 (7.7%)	6.96***
Any type of illness	18 (23.5%)	8 (5.7%)	
6–9	51	32	
Respiratory illness	5 (9.8%)	2 (6.3%)	.07 (ns)
Any type of illness	7 (13.7%)	6 (18.7%)	
0–5	41	38	
Respiratory illness	4 (9.8%)	6 (15.8%)	–.75 (ns)
Any type of illness	5 (12.3%)	6 (15.8%)	

*$p < .10$.
**$p < .06$.
***$p < .01$.
****$p < .001$.

TABLE 2

PREVALENCE OF RESPIRATORY ILLNESS FOR CHILDREN AGED 16 OR UNDER BY DIAGNOSTIC CATEGORY

Kind of Respiratory Illness	Subjected (N = 3,857)	Not subjected (N = 1,953)
Common cold	296 (7.7%)	117 (6.0%)
Other acute upper respiratory illness	14 (0.4%)	3 (0.2%)
Influenza with digestive manifestations	14 (0.4%)	4 (0.2%)
Other influenza	68 (1.8%)	23 (1.2%)
Pneumonia	7 (0.2%)	2 (0.1%)
Bronchitis	7 (0.2%)	3 (0.2%)
Other acute respiratory conditions	13 (0.3%)	2 (0.1%)

Table 2 combines the child data for the three cities by kind of respiratory illness. For each category of respiratory illness, a lower prevalence was obtained for children not subjected to tobacco smoke in the environment (sign test places the probability of 7 out of 7 comparisons favoring the non-smoke-exposed at less than .01).

The question of whether an adult's health is adversely affected by residing with a smoker while not smoking himself gets some answer from the data presented in Table 3. For each city, the health of nonsmokers over the age of 17 residing in a household where one or more of the other members smoked is compared with nonsmokers residing in a smoke-free household. Unfortunately, Detroit was the only location with a large enough sample to enable a reasonable test of the question, and the statistically significant difference favors nonsmokers not subjected to tobacco smoke in the home. As with the children, chronic illness rates were essentially the same for both groups (in Detroit, for instance, the rates were 2.8% and 3.0%).

It will be noted that the percentage of adults subjected to others' household smoke is between 22% and 23% for each location. Respiratory illness rates of smokers approximated those of nonsmokers. In Detroit 7.1% of smokers had a respiratory illness; in Long Beach the figure was 7.4%; while in Pasadena it was 4.5%.

Table 4 compares adult male smokers and nonsmokers residing in Detroit on each of the other items of the questionnaire. The median yearly income and average number in household for Detroit families as reported by the United States Census Bureau is recorded in the last column of Table 4. Clearly our phone-drawn sample was comparable to the census sample. There were essentially no differences in the two populations along any of the dimensions (the mean ages were statistically different and nonsmokers averaged about $200 more income, but neither difference seems large enough to account for the health differences). The "pollution problem" question turned out to be poorly cast and many mentioned water pollution, noise pollution, and the like. Therefore, the equivalent percentages for smokers and nonsmokers suggest equivalent confusion and little else (like Long Beach and Pasadena comparisons similarly yielded no differences).

The hint of an association between amount of tobacco smoke exposure and the prevalence of acute illness for children subjected to smoke uncovered in the last study (Cameron et al., 1969) did not reappear in the present. The biserial correlation between the amount of smoke that sick children under 10 were subjected to versus the amount of smoke

TABLE 3

ACUTE ILLNESS PREVALENCE FOR ADULT NONSMOKER RESIDING WITH TOBACCO SMOKE PRESENT VERSUS ADULT NONSMOKERS RESIDING IN TOBACCO-SMOKE-FREE HOMES

Illness	Subjected (N = 1,179)	Not subjected (N = 1,312)	x^2
Detroit			
Respiratory	80 (6.8%)	73 (5.5%)	
Acute excluding injuries	116 (9.9%)	104 (7.9%)	5.05*
Long Beach			
	(N = 159)	(N = 252)	
Respiratory	10 (6.3%)	12 (4.8%)	
Acute excluding injuries	15 (9.3%)	15 (6.0%)	2.68 (ns)
Pasadena			
	(N = 74)	(N = 143)	
Respiratory	3 (4.0%)	12 (8.4%)	
Acute excluding injuries	5 (6.8%)	17 (11.9%)	−1.13 (ns)

* p < .05

that smokers' well children were subjected to was quite low (.05) and not statistically significant.

The question of a possible differential bias between self-report and other-report of illness prevalence in large samples of families is partially confronted in Table 5. It should be noted that a given adult falls into either the self-or-other-reported side of Table 5; that is, we do not have here a direct comparison of self- versus other-report of illness prevalence for adults from the same families, but rather a comparison of self- versus other-report prevalence rates for adults from different families. Nonetheless, the obvious lack of a difference between the prevalencies reported in the two arrays argues against the notion that self-reported illness prevalences in a random sample of families will differ from other-reported illness prevalences in another random sample of families from the same population. When the data were further broken down into smokers' reports on other smokers' health versus nonsmokers' reports on other smokers' health the same lack of difference appeared. For reports of children's illnesses the same lack of differences was demonstrated for the Detroit, Long Beach and Pasadena data in separate analyses.

About 75% of the interviews were conducted with the woman of the house, while

most of the remainder were conducted with the man of the household. A third of our adult females and 55% of our adult males smoked as compared with 33% and 51% for the United States population of adults (Ahmed & Gleeson, 1970). Thus, about two thirds of our reports were provided by nonsmokers.

Our study also provided a limited test of the notion that respiratory illness rates should be related to the quality of environmental air. The PHS nationwide, and the Air Pollution Control District in Los Angeles, have published estimates of air pollution that would seem to rank the locations involved as follows: Pasadena, most; Detroit, next; and

TABLE 4

DEMOGRAPHIC-ENVIRONMENTAL DIFFERENCES
BETWEEN ADULT DETROIT MALE
SMOKERS AND NONSMOKERS

Demographic factor	Smokers (N = 1,195)	Nonsmokers (N = 1,043)	Detroit population[a]
Average ages	45.0	42.9	
% who regularly take vitamins	33	31	
% who report below average ventilation	2.6	2.5	
% who report a special pollution problem	14	15	
Median yearly income	$7,500-9,999	$7,500-9,999	$8,800
Average number in household	3.9	3.9	4.7

[a] Computed from the 1970 Statistical Abstract of the United States, United States Census Bureau, 1970.

TABLE 5

PREVALENCE OF SELF-REPORTED ILLNESS AND JUDGMENT-OF-ILLNESS BY ANOTHER

Factor	Smokers	Self-report			Report by another		
		Nonsmokers not subjected to second-hand smoke in home	Nonsmokers subjected to second-hand smoke in home	Smokers	Nonsmokers not subjected to second-hand smoke in home	Nonsmokers subjected to second-hand smoke in home	
Acute illness							
Total sample	422	259	203	728	375	322	
With illness	29	17	25	48	30	27	
With illness (%)	6.9%	6.6%	12.3%	6.6%	8.0%	8.4%	
Chronic illness							
With illness	22	12	4	32	9	11	
With illness (%)	5.2%	4.6%	2.0%	4.4%	2.4%	3.4%	

Long Beach, least polluted.[*] If we regard our age-smoke condition groupings (children aged 0–5, 6–9, 10–16 subjected and not subjected to tobacco smoke in the home environment, children who smoke, adults who smoke, adults who do not smoke but are subjected to the same, and adults who do not smoke and are not subjected to smoke) as 10 independent tests of the notion and expect the respiratory illness rate in each group to run lowest in Long Beach and highest in Pasadena, we have 30 predictions and 19 "hits." If we apply Jonckheer's (1954) test to the data (e.g., the first 11 terms of the trinomial expansion $(1\ 2\ 2\ 1)^{10}/6^{10}$ or $8,478,463/60,446,176$), we arrive at a probability of .14. Thus, the data fall in the right direction but fail of statistical significance.

DISCUSSION

The presence of tobacco smoke in the home environment seems to be generally associated with a greater prevalence of respiratory illness in children. The effect has now been found in three rather dissimilar metropolitan areas with varying climates, altitudes, and types of air pollution. The possibility that summer might find the effect diminished is strengthened by the relative weakness of the difference between smoke-subjected and non-smoke-subjected children in the Los Angeles area samples. Even though the time period was the same, in November, Detroit was rather cold and not conducive to outdoor play —the opposite of the climatic conditions in southern California. Because of the pleasant weather, the tobacco smoke in the home was probably less frequently encountered by resident children; thus, both categories of children probably shared outdoor air more frequently in California. It should be noted that most of the children of both samples were not ill at the time of interview. Second-hand tobacco smoke appears to be a significant, but not an all-determining independent variable.

As all our reported research to date has been by phone surveys in metropolitan areas and of the cross-sectional-associational design, it would seem appropriate at this time to mention a piece of longitudinal research done by a graduate student under the direction of the senior author in a rural area of Michigan. Hermann (1965) followed the school absences of the 102 first and fifth graders for the first seven weeks of the fall, 1965, school term in the Hillside Elementary School. She found that the median number of absences ascribed to illness for children subjected to tobacco smoke in the environment ($n = 74$) was higher than for children in smoke-free environments; further, while the median number of half-days absent for children from one-smoker-present families was 0, the corresponding figure for children with two or more smokers in residence ($n = 37$) was 2.

Although non-smoking adults subjected to smoke displayed a statistically greater prevalence of acute illness, it is by no means certain that the finding is a function of the smoke per se. It is possible that the smoke affects their children's health, then the adults "catch" the illness from their children. We will need large samples of smokers with and without children to test this possibility (thus, if we find greater illness among childless non-smokers subjected to smoke, we will have essentially eliminated the latter possibility).

We did not directly confront a possible psychological difference between smokers and nonsmokers that could have generated our results—smokers may be more apt to regard their children as ill at a given intensity of symptoms. That is, smokers may be generally more health-conscious either in general or in regard to their children. Three lines of evidence suggest that this interpretation of our results is not very attractive. First, when the

[*] The Air Pollution Control District of Los Angeles, in a personal communication, reported median single day highs of ozone for each month of the year. The median reading for the West San Gabriel Valley (Pasadena is included here) was .39 while for the South Coastal area (Long Beach) the figure was .17. The United States Department of Health, Education, and Welfare Public Health Service in its August 4, 1967 press release estimated the relative air pollution of the Long Beach-Los Angeles area at 393.5 vs. a 370.0 reading for Detroit. If we assume rough comparability of the two indices (i.e., ozone vs. the PHS conglomerate of various kinds of air pollution), and take at face value that Pasadena is approximately twice as polluted as Long Beach, we would estimate that Pasadena to have a PHS Index of approximately 494 and Long Beach an index rating of approximately 246 in which case the Detroit rating would fall in between.

health data for smoke-subjected children were split into smoker-reported versus nonsmoker-reported prevalences, no statistically significant differences emerged. Though the *same* group of families' health status was not re-indexed using nonsmokers' and smokers' reportage (and the possibility of a reportage-bias still exists), the possibility would seem to be considerably diminished by our finding. Secondly, vitamins have been advertised extensively and are widely believed to be "health-insurance" by the general populace. The essential equivalence of vitamin usage for smoking and non-smoking males (Table 4) (and the same general equivalency obtained for their wives and children) suggests a no-greater health concern among smokers. Lastly, anyone who smokes today must find ways to rationalize or discount mounting scientific opinion that judges his habit health hazardous. While it cannot be maintained that anyone who smokes is *ipso facto* less health conscious, it certainly seems possible that smokers would be somewhat less, rather than more, health conscious. There are other possible differences between the smoke-subjected and non-smoke-subjected families that might have generated some or all of the differences. Among these might be reduced discretionary income (an adult smoker usually spends between $100 and $200/year to maintain his habit) that might otherwise go for superior food products or greater household cleanliness (assuming that either affects health), or greater safety consciousness.

It is likely that many physicians reading this account are puzzled at the lack of a significantly higher rate of illness among adult smokers. We would remind them that sickness is a psychosocial event with no necessary physical parameters. It is undoubtedly true that smokers cough more, that their lung functioning is reduced, etc.; yet, such physical phenomena do not constitute illness—*unless the person involved and/or his interactants judge him ill*. If a person gets used to coughing at a given rate, it makes small difference that most people do not cough that frequently—he is not ill in his own eyes. And

if his family and friends are also used to such a rate for him, he is likewise not sick to them. True, his physiologic functioning may be below average, but there is not necessarily a relationship between illness and physiologic functioning. Thus, if we tested the physiological state of the adult smokers in our sample, we would almost certainly find them below average on many counts; but they and their families are *used* to such a bodily state, and they are simply *not ill* any more frequently. The reason smoking children are most frequently reported ill or report themselves ill is that neither they nor their parents are yet used to their symptoms—predictably both will become used to them and no longer judge the person ill more frequently. Illness, after all, is something only *persons* can have —bodies can deteriorate, machines wear down, *but only people can be sick.*

It would seem profitable to pursue the idea that an association exists between physical health and the quality of environmental air. We are pursuing the possibility that the health differences between smokers' and non-smokers' children will lessen in the summer season.

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Harlap, S., Davies, A.M. "INFANT ADMISSIONS TO HOSPITAL AND MATERNAL SMOKING" The Lancet (March 30, 1974): 529-532.

SUMMARY: Admissions to hospital during the first year of life were recorded in a prospective study of 10,672 infants whose mothers' smoking habits were known. Infants with major congenital malformations, and those dying before their first birthday, were excluded. The infants of mothers who smoked had significantly more admissions for bronchitis or pneumonia, especially in the winter, and more injuries. They were also admitted more frequently, though not significantly so, for upper-respiratory-tract infections, gastroenteritis, childhood infectious diseases, and other diagnoses. The excess of bronchitis and pneumonia in the the group exposed to smoke increased with increasing number of cigarettes smoked by the mother. It occurred within subgroups of birth-weight, social class, and birth order. It was seen mainly in infants aged 6-9 months, while at older and younger ages there was no significant effect of maternal smoking. The findings support the hypothesis that atmospheric pollution with tobacco smoke endangers the health of non-smokers.

INFANT ADMISSIONS TO HOSPITAL AND MATERNAL SMOKING

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Summary   Admissions to hospital during the first year of life were recorded in a prospective study of 10,672 infants whose mothers' smoking habits were known. Infants with major congenital malformations, and those dying before their first birthday, were excluded. The infants of mothers who smoked had significantly more admissions for bronchitis or pneumonia, especially in the winter, and more injuries. They were also admitted more frequently, though not significantly, for upper-respiratory-tract infections, gastroenteritis, childhood infectious diseases, and other diagnoses. The excess of bronchitis and pneumonia in the group exposed to smoke increased with increasing number of cigarettes smoked by the mother. It occurred within subgroups of birth weight, social class, and birth order. It was seen mainly in infants aged 6-9 months, while at older and younger ages there was no significant effect of maternal smoking. The findings support the hypothesis that atmospheric pollution with tobacco smoke endangers the health of non-smokers.

Introduction

CIGARETTE smoking contaminates the atmosphere,[1] and in closed smoke-filled rooms, non-smokers passively inhale smoke components.[2] While non-smokers exposed to tobacco smoke may experience nose and eye irritation, cough, and headache,[3] the relevance of these symptoms to objective measurements of health has not been established.

We have measured the frequency of hospital admissions in a population of West Jerusalem infants whose mothers' smoking habits were known, to test the hypothesis that passive smoking is associated with an increase risk of respiratory disease. In addition, smoking mothers, and their infants, might be more liable to accidents, since (carbon monoxide and other constituents of) tobacco smoke alter sensory and motor function.[4] Furthermore, since smoke pollution in the home should be worse when windows are closed and ventilation reduced, any effect of smoking on morbidity should be greater in winter than in the summer.

In West Jerusalem, hospital inpatient data are a more sensitive index of infant morbidity than in other populations. Paediatrician-G.P. and hospital care are equally available to all, and the reluctance of paediatricians to visit homes added to the availability of hospital beds are associated with hospital-admission rates which are probably the highest in the world.[4] 18% of liveborn infants are admitted at least once before their first birthday, some of them several times, so that the rate of admission episodes is over 25 per 100 liveborn.

Materials and Methods

We have made use of data collected in the record-linked Jerusalem Perinatal Study, described elsewhere.[5] A file, stored on magnetic tape, has been opened for every infant born since 1964 to a mother who lives in West Jerusalem. The file contains information taken from birth certificates and labour-ward books, and is updated with data on deaths and malformations reported from multiple sources.

During 1965-69, all admissions to Jerusalem's three paediatric wards were recorded for infants born since the beginning of the study. The information added to the file included the dates of admission and discharge and the first three diagnoses recorded on the discharge summary, as well as events taking place in hospital and measurements of haemoglobin and weight.

In 1965-68, data from an antenatal interview were added to the file. 68% of pregnant women were interviewed, those attending certain municipal mother-and-child health clinics and hospital-based antenatal clinics. Most interviews were done from the fourth month of pregnancy onwards,[6] and defined indices of health and behaviour were recorded, including details of smoking.

We divided the number of admission episodes to hospital during the first 365 days of life into the following diagnostic categories:

Bronchitis or pneumonia if either or both was among the first three diagnoses recorded on the hospital discharge summary (I.C.D.[7] codes 480, 490-502, 518-529).

Upper-respiratory-tract infections without mention of bronchitis or pneumonia (51, 391-4, 470-9, 481, 510-7).

Gastroenteritis without mention of respiratory infections (40-9, 517-2, 764, 784.1, 785.6).

Other infections and inflammatory diseases, without mention of gastroenteritis or respiratory tract infections (1-39, 50, 52-139, 340-3, 370-9, 400-416, 468, 482-3, 531-2, 536-9, 575-7, 582-3, 590-3, 600, 605, 607, 609, 614, 617.0-.2, 630, 690-9).

Injuries and poisoning regardless of other diagnoses (800-999).

All other diagnoses.

Results

There were 11,350 liveborn infants whose mothers had been interviewed in pregnancy. 678, who had major congenital malformations[8] or died before their first birthday, were excluded, leaving a study population of 10,672. At the time of the interview, 9.2% of the mothers were smokers, and 7.4% had given up smoking earlier. For the total population studied, there were 25.4 admissions per 100 babies aged under 1 year.

The infants of smokers had significantly more admissions to hospital, 30.0% compared with 24.9% for those of non-smokers (table 1). They had higher rates of admissions for bronchitis or pneumonia

TABLE I—ADMISSION-RATES (PER 100 INFANTS) BY DIAGNOSIS AND MATERNAL SMOKING CHARACTERISTICS

Diagnosis	Non-smokers (9686)	Smokers (986)	Total (10,672)
Bronchitis and pneumonia.	9.5	13.1 (P<0.001)	9.8
Upper-respiratory-tract infections...........	4.8	5.3 (N.S.)	4.9
Gastroenteritis...........	6.4	6.5 (N.S.)	6.4
Other infectious diseases...	1.1	1.2 (N.S.)	1.1
Injuries and poisoning....	0.4	1.0 (P<0.01)	0.5
Other....................	2.9	3.1 (N.S.)	2.9
All.....................	24.9	30.0 (P<0.001)	25.4

N.S. = Not significant.

TABLE II—ADMISSION-RATES (PER 100 INFANTS) BY DIAGNOSIS, MATERNAL SMOKING, AND NUMBER OF CIGARETTES SMOKED DAILY

Diagnosis	Non-smokers		Smokers				
	Never smoked (8900)	Former smokers (786)	Cigarettes per day			Total (10,672)	
			1-10 (747)	11-20 (179)	21+ (60)		
Bronchitis and pneumonia....	9.6	7.8	10.8	14.2	31.7	9.8	
All other.........	15.5	15.1	16.4	17.3	23.3	15.6	
Total...........	25.1	22.9	27.2	33.5	55.0	25.4	

Differences among three categories of smokers: for bronchitis and pneumonia, P <0.001, for other diagnoses, not significant.

and more (13.1 per 100) than the infants of non-smokers (9.5 per 100) and more for injuries or poisoning (1.0 v. 0.4 per 100). They also had more upper-respiratory-tract infections, gastroenteritis, infectious and inflammatory diseases, and other diagnoses; though for each of these last four categories the differences between infants of smokers and non-smokers were not statistically significant. Infants born to smokers were in hospital for an average of 384 days per 100 infants before their first birthday, 151 of them for bronchitis or pneumonia. These rates were 334 and 114, respectively, for the infants of non-smokers. However, there were no significant differences between the groups, exposed or not exposed to smoke, in average duration of each type of admission episode.

Admissions for bronchitis or pneumonia increased in frequency with increasing number of cigarettes smoked by the mother (table II). There were no significant increases for any of the other diagnoses measured separately. Infants of mothers who had given up smoking had fewer admissions than those whose mothers had never smoked. This difference, which can be explained by the higher standard-of-living of those who gave up smoking, is not, however, statistically significant for any single diagnostic category. Infants born to former smokers spent fewer days in hospital in the first year of life (231 per 100 infants, 79 of them for bronchitis or pneumonia), and their admission episodes tended to be shorter for each diagnosis.

Women who smoke give birth to smaller infants,[1] and birth-weight is an important predictor of admission to hospital in West Jerusalem.[4] Admissions for bronchitis or pneumonia are more frequent in infants who are smaller or larger than average at birth; while for other diagnoses, increasing birth-weight predicts a decreasing probability of going to hospital. Table III shows that the excess of admissions for bronchitis or pneumonia in the passively smoking infants could not be wholly attributed to lower birth-weights, rates being higher than in the infants of non-smokers for all three birth-weight groups.

Two other important predictors of admission to hospital are social class, based on the husband's occupation, and birth order. In West Jerusalem, smoking mothers tend to be of higher social class, and,

independently of this, they have smaller families. Table IV shows that the effect of maternal smoking on rates of bronchitis or pneumonia was seen within each subgroup of social class. A similar trend was seen for birth order.

The excess of admissions for bronchitis or pneumonia in the group exposed to smoke was greater in the winter than in the summer (table V). For admissions in November to March, the rate in the exposed group was 46% higher than in the infants of non-smokers. For admissions in April to October, the excess was 24%. Of all the winter admissions for bronchitis and pneumonia, 4.2% were due to the effects of maternal smoking, compared to 2.4% of those in summer. Furthermore, for the rates of admissions for bronchitis and pneumonia attributable to smoking in the population as a whole, there was a threefold excess of winter over summer (0.26% compared to 0.08%), again a highly significant difference. These winter-summer differences are independent of small differences between smokers and non-smokers in the distribution of month of birth.

The excess risk associated with maternal smoking was not uniform throughout the first year of life (fig. 1). In the first 5 months of life there were no significant differences between infants born to smokers or non-smokers in rates of admissions for bronchitis or pneumonia. Between the ages of 5 and 9 months, on the other hand, there was an increased rate of lower-respiratory disease in the group exposed to smoke, both in the summer and in the winter. Toward the first birthday, differences between the two groups again disappeared.

The excess of admissions for injuries and poisoning in the infants of mothers who smoked was confined to first-born children (table VI). Although the numbers are small, the differences are most unlikely to be due to chance.
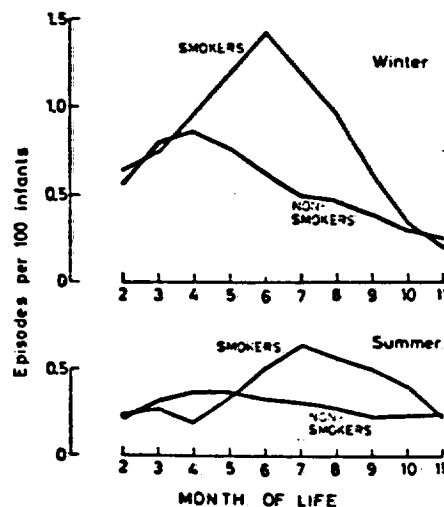
Episodes of bronchitis and pneumonia, winter and summer, in relation to maternal smoking.

TABLE III—ADMISSION-RATES (PER 100 INFANTS) BY DIAGNOSIS, BIRTH-WEIGHT, AND MATERNAL SMOKING

Diagnosis	Birth-weight (g.)						Total (including unknown)	
	≤2999		3000-3499		3500+			
	S (297)	Non-S (2326)	S (415)	Non-S (4098)	S (264)	Non-S (3195)	S (986)	Non-S (9686)
Bronchitis and pneumonia	19.2	12.3	9.6	8.2	12.1	9.0	13.1	9.5
All other	22.6	19.9	14.5	14.6	15.2	13.3	16.9	15.5
Total	41.8	32.2	24.1	22.8	27.3	22.3	30.0	24.9

S=Smokers.   Non-S=Non-smokers.

TABLE IV—ADMISSIONS (PER 100 INFANTS) BY DIAGNOSIS, SOCIAL CLASS, AND MATERNAL SMOKING

Diagnosis	Social class*						Total	
	High		Medium		Low			
	S (392)	Non-S (2644)	S (327)	Non-S (3619)	S (267)	Non-S (3423)	S (986)	Non-S (9686)
Bronchitis and pneumonia	6.6	3.9	15.6	9.0	19.5	14.3	13.1	9.5
All other	10.2	9.3	19.9	13.5	23.2	22.3	16.9	15.5
Total	16.8	13.2	35.5	22.5	42.7	36.6	30.0	24.9

* Ranked by husband's occupation.

TABLE V—ADMISSION-RATES (PER 100 INFANTS) IN WINTER (NOVEMBER-MARCH) AND SUMMER (APRIL-OCTOBER) BY DIAGNOSIS AND MATERNAL SMOKING

Diagnosis	Season	Smoking characteristics of mother			Relative risk (rate for smokers/ rate for non-smokers)	Admissions attributable to smoking (% of total population)
		Non-S	S	Total		
Bronchitis and pneumonia	Winter	6.1	8.9	6.4 ($p < 0.001$)	1.46	0.26
	Summer	3.3	4.2	3.4	1.27	0.08
All other	Winter	5.3	5.5	5.3	1.04	0.01
	Summer	10.2	11.4	10.3	1.12	0.11
Total	Winter	11.4	14.4	11.7 ($p < 0.01$)	1.26	0.27
	Summer	13.5	15.6	13.7	1.16	0.19

Discussion

This study relies on information on maternal smoking which was collected antenatally. It is not known how closely smoking in early pregnancy or mid-pregnancy correlates with habits after the birth and in the baby's first year, but it seems reasonable to asume that for most mothers, smoking characteristics would have remained the same. However, there would inevitably have been some smoking mothers who subsequently gave up the habit, and others, especially former smokers, who took it up later. As a result, this study tends to underestimate true differences between infants of smokers and non-smokers, rather than the opposite.

An unexpected finding was the absence of a significant excess of upper-respiratory-tract infections in the group exposed to smoke. Since smoking causes pathological changes in the upper, as well as lower respiratory tract[1] and upper-respiratory-tract illness is increased in smokers,[10] a measurable excess of upper-tract morbidity was predicted in the passively smoking infants. Hospital inpatient morbidity, however, is a poor indicator of the incidence of upper-respiratory-tract illness since most infants with colds, influenza, pharyngitis, and otitis media would not be admitted. There was a slight excess of hospital admissions in each group exposed to

smoke, not only for upper-respiratory-tract illness but also for gastroenteritis and other diagnoses. This excess, while not statistically significant, was observed consistently within the demographic subgroups, and may represent a small though subtle difference between smokers and non-smokers.

Another unexpected finding was the excess of injuries in the first-borns of smokers. A certain excess was predicted for all birth-order groups, since substances in tobacco smoke may reduce visual and hearing acuity among other indices of sensory and motor function.[1,10] Smokers might, therefore, be more liable to accidents, but why the excess should be confined to first-born babies is not clear. In children under a certain age a proportion of injuries of all birth orders will be due to child abuse,[13] rather than

TABLE VI—ADMISSION-RATES (PER 100 INFANTS) TO HOSPITAL FOR INJURIES AND POISONING, BY BIRTH ORDER AND MATERNAL SMOKING

Birth rank	Non-smokers	Smokers	Total
First-born	7	7	15
	0.3	2.2 ($p < 0.001$)	0.5
Second or later born	31	3	34
	0.4	0.3 (N.S.)	0.4
Total	38	10	49
	0.4	1.0 ($p < 0.01$)	0.5

to accidents, and in this context the interaction between birth order and smoking may be of interest.

This study provides convincing evidence that passive smoking increases acute lower-respiratory-tract disease, at least in infants. The results differ from those of previous studies of parental smoking and child health. Shy et al.[12] studying second-grade schoolchildren, found no relationship between respiratory illness and parental smoking. Cameron et al.[13] on the other hand, did show an excess of acute respiratory illness in children exposed to smoke at home. The excess was only slight, however, in children under 5; it increased with increasing age, and may have been an effect of the children's smoking actively.

This study is consistent with material published recently by Colley et al.[14] Reanalysis of their data shows a significant association between lower-respiratory-tract illness under the age of 2 and smoking at age 20. This association could be mediated through an effect of passive exposure to parents' cigarette smoke in early childhood, since smoking in young adults is correlated with parental smoking.

There is clearly a need for controlled studies in which objective indices of illness are related to measured levels of environmental pollution by cigarette smoke. Meanwhile, it would seem wise to discourage parents from smoking if only for the sake of the health of their children.

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IMPORTANCE OF WARM AND COLD ISCHAEMIA TIMES IN PRIMARY FAILURE OF HUMAN CADAVER KIDNEY TRANSPLANTS

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Summary A retrospective study was undertaken to determine the importance of warm and cold ischaemia times in the transplantation of a hundred and twelve human cadaver kidneys during a 5-year period in the Midlands. Cadaver kidneys with initial warm-ischaemia times of up to 60 minutes were transplanted successfully. Damage sustained during cold ischaemia was one of the major factors in causing the primary failure of a kidney transplant. Cold ischaemia of less than 450 minutes gave a primary-failure rate of 15%. However, when cold ischaemia exceeded 450 minutes the failure-rate increased to 41%. With the present system of ice-containing polystyrene containers used to transport and store kidneys for transplantation, a cold ischaemia of more than $7\frac{1}{2}$ hours is inadvisable.

Introduction

ALTHOUGH ischaemic injury to the kidney during cadaveric renal transplantation is unavoidable, it is the aim of all transplant teams to minimise this injury. In the United Kingdom donor nephrectomy is usually carried out after circulatory arrest has occurred. Warm ischaemia is known to be especially damaging[1] and further ischaemic damage may occur whilst the kidneys are immersed in ice during transportation (cold-ischaemia damage), but the rate at which damage occurs during cold ischaemia is slower than during warm ischaemia.[2] Most British transplant units accept a cold-ischaemia time of as long as 20 hours if the warm-ischaemia time is short—less than 60 minutes. The failure of a transplanted kidney ever to secrete a significant quantity of urine is attributed usually to rejection during the oliguric phase, and the possibility that such a kidney may have been rendered non-viable by prolonged warm or cold ischaemia damage is often overlooked. We have examined the effect of the various ischaemia-times on the fate of a hundred and twelve human cadaver-kidney transplants in an attempt to determine the time limits that are advisable.

Methods

Midlands Kidneys (62)

These were removed from donors using an en-bloc technique.[3,4] The kidneys were separated, each bearing an aortic and a vena caval patch, and flushed through with

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Colley, J.R.T. "Respiratory Symptoms in Children and Parental Smoking and Phlegm Production" British Medical Journal 2: 201-204, 1974.

SUMMARY: A study of respiratory symptoms in 2,426 school children aged 6-14 years was carried out in Aylesbury, Buckinghamshire, in 1971. The prevalence of cough in the children was associated with the parents' smoking habits; prevalence was lowest where both parents were non-smokers, highest where both parents smoked, and lay between these two levels where only one parent smoked. A close association was found between parents' and childrens' respiratory symptoms that was independent of parents' smoking habits. There was no suggestion that exposure to the cigarette smoke generated when parents smoked had any more than a small effect upon the child's respiratory symptoms. While the sharing of genetic susceptibility between parents and children is a factor, therefore, cross infection, particularly in the families where parents smoke, is an important element in the association.

Discussion

Despite the increase in our knowledge and understanding of the pathogenic mechanisms present in patients with diffuse toxic goitre—particularly since the discovery of LATS (Adams, 1958) and its characterization as an immunoglobulin (Adams and Kennedy, 1962; McKenzie, 1962; Kriss et al., 1964; Dorrington et al., 1966)—the cause of the abnormal thyroid function in this disease has remained uncertain. The simplest explanation, and the only one which accounts for the phenomenon of neonatal thyrotoxicosis, is that there is a circulating humoral stimulator acting upon the gland (McKenzie, 1972). Thyrotrophin has been excluded from this role by the fact that its level in blood is less than normal in diffuse toxic goitre (Adams et al., 1969). To many workers LATS has been unacceptable as a causative agent because it is undetectable in many cases and the level in any individual patient does not correlate with the degree of abnormal thyroid function (Volpe et al., 1972). LATS protector, however, meets two criteria not fulfilled by LATS; our evidence confirms the high incidence of LATS protector in diffuse toxic goitre and shows that its serum level correlates well with early thyroid ¹³¹I uptake. Furthermore, LATS protector has been shown to stimulate the human thyroid, both in vitro (Shishiba et al., 1973) and in vivo (Adams et al., 1974). We therefore think that in LATS-negative patients with diffuse toxic goitre LATS protector is the pathogenic agent.

The question whether LATS protector is present in every case of diffuse toxic goitre remains open. It was not found in five of the 50 patients studied, but all these were relatively mild cases with normal or only slightly raised thyroid ¹³¹I uptake and large goitres. Failure to detect LATS protector in these inactive cases may have been due to assay insensitivity, but incorrect diagnosis of thyrotoxicosis or an alternative pathogenic mechanism for thyroid dysfunction are other possible explanations.

The pathogenesis of the ophthalmopathy of Graves's disease remains less well understood than the pathogenesis of thyrotoxicosis. We found no significant correlation between the class of ophthalmopathy and the LATS protector level. The highest incidence of infiltrative ophthalmopathy, however, was observed in the group of patients with both LATS and LATS protector, and the lowest incidence was in those patients in whom neither immunoglobulin could be detected. Our findings support the view that LATS protector and ophthalmopathy may be associated in Graves's disease but the relation is not a causal one.

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Respiratory Symptoms in Children and Parental Smoking and Phlegm Production

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Summary

A study of respiratory symptoms in 2,426 schoolchildren aged 6-14 years was carried out in Aylesbury, Buckinghamshire, in 1971. The prevalence of cough in the children was associated with ~~~~~~ between these two levels ~~~~~~~~~~ ~~~~~~~~~~~~~~~~~~~. A close association was found between parents' and children's respiratory symptoms that was independent of parents' smoking habits. There was no suggestion that exposure to the cigarette smoke generated when parents smoked had any more than a small effect upon the child's respiratory symptoms. While the sharing of genetic susceptibility between parents and children is a factor, therefore, cross infection, particularly in the families where parents ~~smoke~~ is an important element in the association.

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Introduction

Norman-Taylor and Dickinson (1972) suggested that children with parents who smoke may be at particular risk from respiratory disease. These authors were not, however, explicit about the nature of the risk. They implied that exposure of children to cigarette smoke at home might increase the risk of respiratory illness. This paper reports the findings of a study in which the nature of the association between parental smoking and respiratory disease in their children was investigated.

Methods

The material was collected during a study of the prevalence of respiratory disease in schoolchildren and their parents in Aylesbury, Buckinghamshire, in 1971. The population consisted of all children aged 6-14 years attending seven schools in Aylesbury—a total of 2,598 children (1,328 boys and 1,270 girls). Data were collected on 2,426 children and their parents, a response rate of 93.4%.

A self-administered questionnaire was completed by the parents, who answered questions about their own and their

children's health. The relevant questions were: (a) for each child, Does he/she usually cough during the day or at night in the winter?; (b) for each parent, (1) Do you usually bring up any phlegm from your chest first thing in the morning in winter?; (2 a) Do you smoke? If "No"; (2 b) Have you ever smoked as much as one cigarette a day for as long as a year? Parents who answered "Yes" to question (2 a) were classified as smokers. They were also asked how many cigarettes they smoked a day, how many ounces of tobacco they smoked each week, and how many cigars, large and small, they smoked each week. Those parents that answered "No" to question (2 a) and answered question (2 b) in the negative were classified as non-smokers, while those that responded in the affirmative to question (2 b) were classified as ex-smokers. The validity of the question on cough in the children when used in a self-administered questionnaire has already been established (Colley and Reid, 1970), as has that of the question on phlegm production (Krueger et al., 1970).

The father was asked about his occupation and from this his social class was obtained. (Classification of Occupation, 1970). The number of siblings which the index child had was also recorded.

Results

The relation in the parents between smoking habits and prevalence of phlegm was what one would have expected; prevalence rose with amount smoked. Parents were classified by smoking habit into five groups; group 1, both parents non-smokers; group 2, one parent a smoker, the other a non-smoker; group 3, both parents smokers; group 4, both parents ex-smokers or one an ex-smoker and the other a non-smoker or smoker; and group 5, one or both parents gave no data on smoking habits. Within these five groups the prevalence in the children of cough during the day or at night in the winter was determined (table I). The cough prevalence rates were lowest

in children with one or both parents ex-smokers. The gradient in prevalence over groups 1, 2, and 3 was statistically significant (x^2 for trend 6·865; 0·01 > P > 0·005). The findings indicated an association between parental smoking habits and the prevalence of symptoms in their children.

The analysis was taken a stage further by classifying parents by both smoking habits and by their response to the question, Do you usually bring up any phlegm from your chest first thing in the morning in winter? (table II). Within each group the prevalence of cough in children was lowest among children of parents who did not report symptoms. It was highest in those children where both parents reported symptoms. Where only one parent reported the symptom the prevalence rate lay between these two extremes. Overall, there was a threefold difference in prevalence of cough between children with neither parent having the symptoms and both having the symptom.

Some of the prevalence rates in table II were based on small numbers, but the numbers in the category where neither parent had symptoms allowed a firmer conclusion. It was thus interesting to note that in this category the prevalence of cough rose from 12·4% in children of non-smoking parents to 14·3% where one parent smoked and to 14·7% where both smoked. This trend while small and not statistically significant nevertheless raised the possibility that exposure to cigarette smoke at home when parents smoked might have had some effect on the child's respiratory tract. A more precise estimate of the effects of "passive smoking" by the child was obtained by estimating the maximum daily exposure of the child to their parents' cigarette smoke. This was derived by the addition of both parents' daily cigarette consumption. Among the children of parents who did not have morning phlegm there was a small gradient for cough prevalence according to the number of cigarettes (or tobacco equivalent) smoked by the parents (table III). This gradient in prevalence is not, however, statistically significant (x^2 trend 1·36; 0·30 > P > 0·20).

TABLE I—Prevalence of Cough during Day or at Night in Winter in Children aged 6-14 according to Parents' Smoking Habits

	Parents' Smoking Group*					Total†
	1	2	3	4	5	
Percentage (No.) of children with cough	15·6 (320)	17·7 (547)	22·2 (634)	14·2 (620)	20·7 (217)	18·0 (2,338)

*See text for composition of groups.
†Total excludes 83 children for whom there were no data on cough.

TABLE II—Prevalence of Cough during Day or at Night in Winter in Children aged 6-14 according to Parents Smoking Habits and Presence of Winter Morning Phlegm

Winter morning phlegm in parents	Group 1			Group 2			Group 3			Group 4			Total*		
	Neither	One	Both	Neither	One	Both	Neither	One	Both	Neither	One	Both	Neither	One	Both
Percentage (No.) of children with cough	12·4 (274)	27·5 (40)	80·0 (5)	14·3 (420)	24·7 (97)	52·9 (17)	14·7 (309)	24·1 (156)	41·5 (69)	12·6 (499)	19·4 (98)	23·1 (13)	13·5 (1,582)	25·1 (394)	44·2 (104)

*Total excludes 346 children for whom there were no data on cough or parents' smoking habits or morning phlegm.

TABLE III—Prevalence of Cough during Day or at Night in Winter in Children aged 6-14 according to Parents Smoking Habits, Number of Cigarettes smoked, and Presence of Winter Morning Phlegm

	Group 1		Groups 2 and 3								Group 4		Total†	
			Total No. of Cigarettes*											
			1-9		10-19		20-29		>30					
Winter morning phlegm in parents	N	O/B	N	O/B	N	O/B	N	O/B	N	O/B	N	O/B	N	O/B
Percentage (No.) of children with cough	12·4 (274)	33·3 (45)	13·3 (135)	32·1 (28)	13·8 (247)	21·3 (65)	14·9 (208)	37·8 (74)	15·9 (208)	32·2 (174)	12·6 (499)	19·8 (111)	13·56 (1,571)	28·97 (497)

N = Neither. O/B = One or both.
*Including tobacco and cigars expressed as cigarette equivalents (see Todd, 1972).
†Total excludes 358 children for whom there were no data on cough or parents' smoking habits or morning phlegm.

Several points have to be considered in interpreting these findings. As in other studies (Holland et al., 1969; Colley and Reid, 1970), social class gradients for respiratory symptoms in children were found in this series. Children with fathers in semi-skilled and unskilled occupations had higher prevalence rates for respiratory symptoms than those whose fathers were in skilled or non-manual occupations. A concentration of low social class families in the groups where both parents reported winter morning phlegm could have produced a similar pattern to that shown in table II. That this could not have accounted for the observed patterns of cough prevalence in the children may be seen in table IV, where cough prevalence is given for children in social class III according to the parents' history of phlegm production after standardization for smoking. Cough prevalence in the children increased, as before, with the presence of parental phlegm production.

TABLE IV—Prevalence in Social Class III of Cough during Day or at Night in Winter in Children aged 6-14 according to Parents' Phlegm (Standardized for Parents' Smoking Habits)

Parents with winter morning phlegm ..	Neither	One	Both
Percentage (No.) of children with cough ..	15·4 (824)	27·4 (207)	52·9 (54)

Children from large families have higher prevalence rates for respiratory symptoms than those from small families (Colley, 1970), and a concentration of large families in the groups of parents with symptoms might also have resulted in the prevalence of morning cough being similar to that shown in table II. It can be seen from table V, however, that within families of similar size the same gradients for cough prevalence according to parents' phlegm production were present, indicating that differences in the number of siblings could not have explained the gradient in cough prevalence.

TABLE V—Prevalence of Cough during Day or at Night in Winter in Children aged 6-14 according to Parents' Phlegm and Number of Siblings (Standardized for Parents' Smoking Habits)

Parents with Winter Morning Phlegm	No. of Siblings					
	Nil or 1		2		3 or More	
	No. of Children	Prevalence (%)	No. of Children	Prevalence (%)	No. of Children	Prevalence (%)
Neither	672	14·2	444	11·6	464	14·8
One	122	16·5	137	27·6	135	27·4
Both	25	37·9	27	37·5	52	44·4

Table excludes 348 children owing to lack of data on cough, or on parents' smoking habits or morning phlegm, or on family size.

Younger school children tend to have higher prevalence rates for winter cough than older children (Colley and Reid, 1970). If the age distributions of children in the various groups in table II had not been the same prevalence rates between these groups might also have differed, but there were no differences in age structure between these groups of children.

Conclusions drawn from the evidence in this study need to be viewed with caution because it was not possible to collect evidence which would have excluded some other interpretation of the results. It was possible, for example, that the parents' account of their own symptoms might have influenced the answers they gave for their children and that the apparent association between parents and children in their respiratory experience could have been due to parents with symptoms over-reporting symptoms in their children. The children of parents who smoked may also have been more likely to have smoked than children of non-smoking parents, and this could have resulted in an increased prevalence of cough in such children. If either of these possibilities had oc-

curred to any material extent it would have meant that, as given in table II the prevalence of cough in children from group 2 was too high in relation to cough in children from group 1 and that the prevalence of cough in children from group 3 was still higher. If the prevalence of cough in children from group 2 were to be reduced in order to correct for this and that of children from group 3 were to be corrected even more then the gradient shown in table II would probably become negative in that cough prevalence in children would have seemed to decline as more parents smoked. It therefore seems reasonable to conclude that the two possible qualifications to the data did not operate.

Discussion

Norman-Taylor and Dickinson (1972) in their study of children's respiratory infections and parental smoking habits reported higher prevalence rates for various indices of respiratory disease among children with parents who smoke. The present study, using a single index of respiratory disease, confirms their findings. It can now be seen, however, that a direct association exists between respiratory symptoms in parents and in their children. Parental smoking has a mainly indirect effect on the child by increasing the prevalence of the parental respiratory symptoms and thus the prevalence of respiratory symptoms in their children. The direct effect on the children's respiratory symptoms of exposure to the smoke generated when their parents smoked cigarettes seemed to be relatively small.

The reason for the association between respiratory symptoms in parent and child is not clear. The sharing of genetic susceptibility between parents and children could have led to these similarities in respiratory disease, but this is unlikely to be the whole explanation, particularly in families where both parents smoke. There is, for example, no convincing evidence that adults who take up smoking have a greater genetic susceptibility to respiratory disease than non-smokers, and therefore there is no reason to suppose that susceptibility to respiratory disease would be different in the children of smokers and non-smokers. On the other hand, smoking parents differed from the nonsmokers in that they had higher prevalence rates for respiratory symptoms and the rates rose with the amount smoked, indicating some direct effect of smoking in causing their symptoms. In these circumstances the association between parents' and children's symptoms are more likely to be due to cross infection than to the sharing of genetic susceptibility.

If cross infection is indeed an important cause of respiratory symptoms in children of parents with symptoms then there could well be some advantage to their children if the parents gave up the habit. In adults giving up smoking can result in a reduction in cough and expectoration and, therefore, in the chance of transmitting respiratory infections. Smoking parents, many of whom will not yet have developed severe or irreversible respiratory damage, can reasonably expect an improvement in symptoms if they give up the habit, and this would offer a promising way of reducing the risk of their children developing respiratory symptoms.

The findings in this paper need confirmation. This could be done by prevalence studies on a larger scale in other populations where, for example such aspects as the possible over-reporting of symptoms could be adequately investigated. There is a need to investigate the likely benefit to the child from parents giving up smoking. Though passive inhalation of cigarette smoke by the child has not been shown to have an important effect in this series, this aspect should nevertheless be studied in infants and preschool children who tend to be the most susceptible to respiratory infections.

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Choreo-athetosis and Encephalopathy Induced by Phenytoin

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Summary

Two patients with intractable epilepsy who had been treated with various combinations of anticonvulsant drugs developed phenytoin encephalopathy. In both patients choreo-athetoid involuntary movements were prominent. Blood phenytoin concentrations were above 50 µg/ml. When phenytoin was given in smaller doses and its level in the blood fell the involuntary movements and other clinical manifestations disappeared.

Introduction

Nystagmus, ataxia, dizziness, and drowsiness are well-known features of phenytoin toxicity which usually occur when the blood level is greater than 20 µg/ml (Buchthal et al., 1960). There have been few reports of other toxic effects on the central nervous system though Glaser (1973) pointed out that a reversible encephalopathy may occur in some patients treated with large doses of the drug. We describe two patients in whom choreo-athetoid involuntary movements were a prominent and presenting feature and in whom the involuntary movements and the encephalopathy were closely correlated with very high blood phenytoin concentrations.

Case Reports

CASE 1

A 31-year-old man who had attended hospital for many years for management of epilepsy was admitted for investigation of involuntary movements and intractable seizures. He had had a febrile convulsion when 2 years old and had had recurrent petit mal and major generalized seizures since he was 7. An electroencephalogram when he was aged 13 showed typical, generalized, three-per-second spike-and-wave complexes and diffuse bursts of theta and delta activity. When assessed for industrial training when aged 21 he had an I.Q. of 84 on the Wechsler Intelligence Scale. He was treated with various combinations of anticonvulsants,

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including troxidone, ethosuximide, primidone, and phenytoin, but he continued to have two or three major seizures a month. When he was aged 29 Hodgkin's disease was diagnosed by biopsy of an enlarged cervical lymph node. No involvement of liver, spleen, or para-aortic nodes was seen on laparotomy and he was treated with radiotherapy to the neck. There had been no recurrence. Treatment with phenytoin 300 mg, phenobarbitone 150 mg, and ethosuximide 750 mg daily was continued. Two years later the seizures became more frequent (two to four a week) and primidone 750 mg, carbamazepine 800 mg, and phenytoin 450 mg daily were gradually substituted for the previous treatment. During the next six weeks he complained of blurred vision and ataxia, leading to frequent falls. He continued to take the drugs. The seizures continued unchanged.

On admission to hospital he was slightly drowsy but orientated. Several minor seizures were observed. He had grade I nystagmus in all directions and upward conjugate gaze was impaired. There was generalized chorea which was present at rest and was enhanced by movement, particularly by walking. Slurred and hesitant speech seemed to be due to interposed choreic movements of the lips and tongue. In the outstretched upper limbs choreiform involuntary movements were accompanied by irregular postural lapses of the fingers, which were thought to be typical of asterixis rather than chorea. The gait was unsteady, but there were no cerebellar signs in the limbs. There was no weakness or sensory impairment, the tendon reflexes were brisk, and both plantar responses were flexor. Hyperplasia of the gums was noted. The increased frequency of seizures and the encephalopathy with involuntary movements were first ascribed to a degenerative or infective disorder associated with the Hodgkin's disease. The haemoglobin, white cell count, E.S.R., liver function tests, blood urea and electrolytes, skull and chest x-ray examinations, and brain scan were normal. The background activity in the E.E.G. was fragmented and slowed and there was an excess of diffuse, irregular delta activity of moderate voltage. Generalized atypical spike-and-wave activity was prominent. The blood phenytoin concentration was 37 µg/ml.

The possibility of phenytoin encephalopathy was considered. The daily dose of phenytoin was reduced to 200 mg daily and that of primidone increased to 1 g. Carbamazepine 800 mg daily was continued. During the next six days the patient became more alert, the chorea, ataxia, and nystagmus disappeared, and the blood phenytoin level fell to 16 µg/ml. The seizures at first increased in frequency but then abated. Three weeks later he returned to work. Neurological findings at that time were normal.

CASE 2

This 15-year-old boy was referred for management of uncontrolled epilepsy. He had had frequent minor and major seizures since the age of 2 when he had presented in status epilepticus. He had been treated with varying combinations of phenytoin, phenobarbitone, ethosuximide, and sulthiame and had been almost free

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INFLUENCE OF PASSIVE SMOKING AND PARENTAL PHLEGM ON PNEUMONIA AND BRONCHITIS IN EARLY CHILDHOOD

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Summary The incidence of pneumonia and bronchitis has been studied in 2205 infants over the first five years of life. In the same period their parents' smoking habits and respiratory symptoms were recorded annually. The incidence of pneumonia and bronchitis in the first year of life was associated with parents' smoking habits; incidence was lowest when both parents were non-smokers, highest where both smoked, and lay between these two levels where only one parent smoked. Over the age of one year the association was not consistent. When parents' respiratory symptoms were also studied a close association was found with the incidence of pneumonia and bronchitis in the child; this was independent of parents' smoking habits and was an almost consistent finding throughout the first five years of life. In the first year of life exposure to cigarette smoke generated when parents smoked doubled the risk for the infant of an attack of pneumonia or bronchitis.

Introduction

INFANTS who inhale the tobacco smoke generated when their parents smoke at home may have a greater risk of chest illness than the infants of non-smoking parents. We have studied the influence of parental smoking and respiratory symptoms for effects on the incidence of pneumonia and bronchitis in their children during the first five years of life.

Methods

The data that form the basis of this paper are part of those collected during a longitudinal study of newborn infants and their families. The study was conducted in Harrow, a borough in north-west London, between 1963 and 1969 and involved all families living in six of the wards of the borough who had an infant born in the period July 1, 1963, to June 30, 1965. A total of 2365 families had newborn infants during this period, and, of these, 2205 (93%) were included in the study. The 6·8% excluded (i.e., 160 families) had either moved away from the area before they could be visited or refused to cooperate in the study (table 1). The analysis that follows has been based upon the infants born to these families. After exclusions—for example, multiple births—2149 infants were eligible for study. Over the five years of follow-up losses inevitably occurred from the original population; these were small and are unlikely to have seriously biased the findings in the later years of follow-up.

Health visitors, who received special training, administered a questionary to the parents, when, as part of their

TABLE I—SURVEY POPULATION OVER THE FIVE YEARS OF FOLLOW-UP

No. of families with newborn infants born July 1, 1963, to June 30, 1965		No. of index infants at annual follow-up					
Total	Cooperated in survey	Initial visit	First	Second	Third	Fourth	Fifth
2365	2205	2149	2122	2109	2096	2097	2095

routine duties, they visited the infant and mother at home within fourteen days of the delivery. At this visit a number of items were recorded, including birth-weight in pounds to the nearest pound below.

The health visitor also administered a questionary which included questions on respiratory symptoms and smoking habits. In this paper positive responses to the question "Do you usually bring up any phlegm from your chest first thing in the morning in the winter?" has been used as evidence for parental respiratory disability. To elicit smoking habits the questions were: "Do you smoke?" If answered "yes", the parent was classified as a present smoker. If answered "no" the parent was asked "Have you ever smoked?" If the answer was "yes", then the parent was classified as an ex-smoker. If answered "no" the parent was asked "Have you ever smoked as much as one cigarette a day for as long as a year?" An answer "no" classified parents as non-smokers. The present smokers were also asked "How many cigarettes are you smoking now?" The validity of the answers to these questions has already been established.[1]

The families were followed up annually for the next five years by postal questionaries. Each year parents were asked the following questions. For the infant, "Has he/she had in the past twelve months bronchitis? Pneumonia?" For the parents, "Did you usually bring up any phlegm from your chest first thing in the morning last winter?" Smoking habits were assessed using the question "Do you smoke?" If "yes", "How many are

you smoking now?" The validity of answers to the question on infant bronchitis and pneumonia was assessed by checking, in a sample, the parents' account of such an illness with the family doctor's case-notes. The level of agreement was adequate and corresponded to that obtained in other studies where mothers were asked about their children's past health. The validity of the question on phlegm production in the parents has also been established.[2]

In the tables that follow, parents have been classified according to their smoking habits. Parents who at the initial visit had never smoked, and at the first and subsequent follow-ups had not taken up the habit, were classified at each follow-up as non-smokers. In the same way parents who at the initial visit were present smokers, and at the first and subsequent follow-ups did not give up the habit, were classified on each occasion as present smokers. There remained a further group of parents who had changed their habits. These included parents who at the initial visit were ex-smokers. They had been permanently allocated, irrespective of whether or not they took up smoking again, to the "ex-smokers or changed habits" group. In addition there is a further group of parents who were either non-smokers or smokers at the initial visit but who changed their habits during their follow-up. When this occurred they were reclassified permanently as members of the "ex-smokers or changed habits" group. In this way, for example, parents who were smokers at the initial and first and second follow-up visits would be classified as such at these follow-ups. If on the third follow-up they gave up smoking they would be moved to the "ex-smoker or changed habits" group for that and subsequent follow-up years. This method of classification ensures that at each follow-up year the group of "non-smoking" and "present smoking" parents contains parents with consistent smoking habits. The diminishing numbers at each follow-up in these two groups is a result of parents changing their habits and is balanced by the increasing numbers in the "ex-smokers and changed habits" group. The totals in these tables do not correspond to those in table 1. This is accounted for by the exclusion of single-parent families and by absent data.

Results

The annual incidence per 100 children of pneumonia and bronchitis is given in table II by parents' smoking habit. Parents have been classified into one of four groups: (1) both parents non-smokers; (2) one parent smoker, the other non-smoker; (3) both parents smokers; (4) both parents ex-smokers, or one an ex-smoker, or parents who changed their smoking habits during the study. The incidence of pneumonia and

bronchitis in the infant shows a gradient by parents' smoking habit in the first year of life. Incidence is lowest in infants with both parents non-smokers, highest where both parents smoke, and lies between these values where one parent smokes. This is a statistically significant gradient $(p < 0.0005)$.[1] In subsequent years there is no such clear gradient.

In table III parents have been classified both by their smoking habits and by their response to the question "Did you usually bring up any phlegm from your chest first thing in the morning in the last winter?" In all categories except one, the incidence within a smoking category is higher among children where one or both parents have winter morning phlegm than in children whose parents are both free of this symptom. Some of the incidence-rates in the children—in particular those whose parents are both non-smokers and who have winter morning phlegm—are based upon small numbers and therefore may not be wholly reliable. On the other hand, the incidence-rates in children where neither parent has symptoms, whether they smoke or not, are based upon substantial numbers. In them in the first year of life a consistent gradient is seen in the incidence of pneumonia and bronchitis in the children in relation to the parents' smoking habits. The rates are lowest in children of non-smoking parents and highest where

TABLE II—PNEUMONIA AND BRONCHITIS BY PARENTS' SMOKING HABITS

Year of follow-up	Annual incidence per 100 children (absolute numbers in parentheses) of pneumonia and bronchitis				
	Both non-smokers	One smoker	Both smokers	Both ex-smokers or one ex-smoker or smoking habit changed	All
1	7·8 (372)	11·4 (552)	17·6 (478)	9·2 (675)	11·5 (2077)
2	8·1 (358)	9·3 (494)	8·9 (438)	7·4 (758)	8·3 (2048)
3	7·0 (342)	10·2 (460)	9·1 (396)	8·9 (834)	8·9 (2032)
4	8·4 (323)	8·3 (408)	9·0 (357)	8·1 (882)	8·5 (1970)
5	7·5 (319)	6·7 (374)	6·5 (340)	6·6 (956)	6·7 (1989)

TABLE III—PNEUMONIA AND BRONCHITIS IN THE FIRST FIVE YEARS OF LIFE BY PARENTS' SMOKING HABIT AND MORNING PHLEGM

Year of follow-up	Annual incidence per 100 children (absolute numbers in parentheses) of pneumonia and bronchitis									
	Both non-smokers		One smoker		Both smokers		Both ex-smokers or one ex-smoker or smoking habit changed		All	
	N	o/s	N	o/s	N	o/s	N	o/s	N	o/s
1	7·6 (343)	10·3 (29)	10·4 (424)	14·8 (128)	15·3 (339)	23·0 (139)	8·2 (546)	13·2 (129)	10·1 (1652)	16·7 (425)
2	8·1 (322)	8·3 (36)	7·1 (365)	15·5 (129)	8·7 (286)	9·2 (152)	6·5 (599)	10·7 (159)	7·4 (1572)	11·3 (476)
3	6·9 (305)	8·1 (37)	10·5 (353)	9·4 (107)	7·9 (242)	11·0 (154)	8·2 (661)	11·6 (173)	8·4 (1561)	10·6 (471)
4	8·0 (287)	11·1 (36)	7·5 (306)	10·8 (102)	7·6 (236)	11·6 (121)	8·2 (695)	9·1 (187)	7·9 (1524)	10·3 (446)
5	6·7 (285)	14·7 (34)	5·6 (267)	9·4 (107)	3·9 (208)	10·6 (132)	6·4 (737)	7·3 (219)	5·9 (1497)	9·1 (492)

N = neither with winter morning phlegm.   o/s = one or both with winter morning phlegm.

TABLE IV—PNEUMONIA AND BRONCHITIS BY NUMBER OF CIGARETTES SMOKED PER DAY BY PARENTS AND WINTER MORNING PHLEGM

Year of follow-up	Annual incidence per 100 children (absolute numbers in parentheses) of pneumonia and bronchitis							
	Both non-smokers		One or both smokers* of following number of cigarettes per day†:					
			1-14		15-24		25 and over	
	N	o/b	N	o/b	N	o/b	N	o/b
1	7·6 (343)	10·3 (29)	10·4 (269)	15·1 (53)	11·1 (171)	14·5 (76)	15·2 (323)	23·2 (138)
2	8·1 (322)	8·3 (36)	5·2 (231)	16·4 (55)	8·6 (151)	14·5 (62)	9·7 (269)	9·8 (164)
3	6·9 (305)	8·1 (37)	11·2 (206)	8·6 (58)	8·2 (146)	9·5 (42)	8·6 (243)	11·2 (161)
4	8·0 (287)	11·1 (36)	5·5 (163)	13·3 (45)	7·4 (136)	11·5 (52)	9·1 (243)	10·3 (126)
5	6·7 (285)	14·7 (34)	6·3 (144)	11·4 (44)	4·4 (113)	7·6 (53)	4·1 (218)	10·6 (142)

* Excluding parent pairs where one or both are ex-smokers or changed smoking habit.
† Includes tobacco and cigars expressed as cigarette equivalents (see Todd ¹¹).
N=neither with winter morning phlegm.   o/b=one or both with winter morning phlegm.

both parents smoke. In children over the age of a year there is, however, no consistent gradient.

Exposure of the child to cigarette smoke may be more precisely estimated from the total daily cigarette consumption of both parents. In table IV the incidence of pneumonia and bronchitis is given for parent pairs smoking between them 1-14, 15-24, and 25 or more cigarettes per day, by the presence of winter morning phlegm. A clear gradient of increasing incidence is seen in the first year of life that is independent of the presence of winter morning phlegm and is of the same size as that in table III. In the second year and thereafter the pattern is not consistent and thus does not suggest an effect of exposure to tobacco smoke at ages over one year.

The gradients of incidence, particularly those attributable to passive smoking in the first year of life, could result from other factors which are known to influence respiratory disease in infancy—for example, social class and family size. These factors might account for the gradients if children of low social class or of large family size were concentrated in families where the parents smoked or had chest symptoms. That these factors did not explain the observed gradient can be seen in tables V and VI. In table V, the findings for social class III alone are

examined. The patterns for pneumonia and bronchitis for all children in the first year of life persist. Similarly, in table VI, where the data are subdivided by the number of siblings in the family, the patterns for pneumonia and bronchitis persist within families of the same size. This makes it unlikely that either social class or family size can be responsible for these patterns of respiratory-disease incidence.

The infants of mothers who smoke in pregnancy are, on average, lighter than those of mothers who do not smoke.³ As infants of low birth-weight are more likely to suffer respiratory illness than normal-weight infants, it is possible that the gradients in respiratory disease observed in the first year of life, and in particular the effects of passive smoking, may be due, indirectly, to maternal smoking during pregnancy. In this study, birth-weight, as expected, shows a

TABLE V—PNEUMONIA AND BRONCHITIS IN THE FIRST YEAR BY PARENTS' SMOKING HABIT AND WINTER MORNING PHLEGM FOR SOCIAL CLASS III

Annual incidence per 100 children (absolute numbers in parentheses) of pneumonia and bronchitis									
Both non-smokers		One smoker		Both smokers		Both ex-smokers or one ex-smoker		All	
N	o/b	N	o/b	N	o/b	N	o/b	N	o/b
5·9 (171)	20·0 (15)	9·5 (263)	16·5 (79)	17·1 (217)	23·9 (88)	7·1 (294)	12·1 (66)	9·8 (945)	18·2 (248)

N=neither with winter morning phlegm.   o/b=one or both with winter morning phlegm.

gradient by parents' initial smoking habit, and to a lesser extent by winter morning phlegm. Thus parents who smoke have lighter infants than parents who do not smoke. The gradients in the incidence of pneumonia and bronchitis with parental smoking, and with winter morning phlegm, might therefore be partly attributable to differences in birth-weight. However, within different birth-weight categories the gradients for pneumonia and bronchitis with parents' smoking habits persist. Thus differences in birth-weight cannot account for the higher risk of pneumonia and bronchitis in the first year of life in children exposed to the cigarette smoke generated when their parents smoke at home.

Discussion

An association between the respiratory symptoms

TABLE VI—PNEUMONIA AND BRONCHITIS IN THE FIRST YEAR BY NUMBER OF SIBLINGS AND BY PARENTS' SMOKING HABIT AND WINTER MORNING PHLEGM

No. of siblings	Annual incidence per 100 children (absolute numbers in parentheses) of pneumonia and bronchitis									
	Both non-smokers		One smoker		Both smokers		Both ex-smokers or one ex-smoker or smoking habit changed		All	
	N	o/b	N	o/b	N	o/b	N	o/b	N	o/b
0	3·9 (153)	14·3 (14)	5·1 (177)	6·3 (32)	13·3 (165)	12·7 (55)	5·8 (258)	6·4 (47)	6·9 (753)	9·5 (148)
1	8·1 (124)	0 (7)	13·0 (146)	12·0 (50)	13·6 (103)	34·1 (44)	9·6 (178)	17·5 (40)	10·9 (551)	19·9 (141)
2 and more	15·2 (66)	12·5 (8)	15·8 (101)	23·9 (46)	22·5 (71)	25·0 (40)	11·8 (110)	16·7 (42)	15·8 (348)	21·3 (136)

N=neither with winter morning phlegm.   o/b=one or both with winter morning phlegm.

in parents and in their school-age children was reported by Colley.[1] The present study demonstrates that this association is also found in younger children as early as the first year of life. The nature of this association, as Colley noted, is not clear. He concluded that it was unlikely to be an artefact due, for example, to parents with symptoms over-reporting symptoms in their children. In the present study a sample of parents had their account of respiratory illnesses in their children checked against the doctors' records. The close agreement between these two accounts makes it unlikely that over-reporting in families where parents have symptoms has occurred to any important extent.

The association could be a result of shared genetic susceptibility to respiratory disease between parents and children, to living in the same home environment, and to cross-infection within the family. Twin studies in adults have not been notably successful in assessing the genetic contribution to adult chronic respiratory disease, and no studies have yet been reported where this aspect was investigated in parents and their children. The contribution made by the other factors to this association can, at present, only be guessed at.

Passive smoking by the infant, after differences in birth-weight and parental respiratory symptoms have been allowed for, increases the risk to the infant of pneumonia and bronchitis in the first year of life. When both parents smoke, this risk is almost double that of infants with non-smoking parents. The findings confirm and extend those of Harlap and Davies.[5] These workers did not, however, have information on fathers' smoking habits, nor did they take account of parents' respiratory symptoms.

A picture has thus emerged of a serious risk to infants in the first year of life from exposure to their parents' cigarette smoke. In contrast, between one and five years of age, there does not appear to be any important effect of passive smoking in increasing the risk of pneumonia and bronchitis. Colley,[4] in 6–14-year-olds also found no association between passive smoking and the prevalence of chronic cough. The estimates of children's exposure to cigarette smoke in this study are crude, being based either on whether parents were smokers or not, or on their total daily cigarette consumption. The smoke exposure of the children may have been overestimated, since parents—in particular the father—will smoke outside the home, or at times when the infant is not present. The effects on the child may thus have resulted from exposure to levels of cigarette smoke less than those suggested by our study.

The evidence from this study, taken with that of Harlap and Davies,[5] provides convincing reasons for warning parents who smoke of the risks this entails for their children both from the direct effect of their cigarette smoke and from the presence of their respiratory symptoms. Attacks of pneumonia and bronchitis, particularly in the first year of life, can still result in infant death despite prompt and vigorous treatment. In those that survive such illnesses and recover clinically, the evidence points to some damage to the respiratory tract as indicated by an increased prevalence of chest symptoms and deficient ventilatory function found in later childhood.[6-8] The

longer-term consequences of such childhood illnesses have been underlined by the findings in a cohort of infants followed to the age of 20.[9] At this age the prevalence of chronic cough, after allowing for current smoking habits, social class of father, and air-pollution exposure, was higher in those with a documented history of a chest illness under the age of 2 years than in those without this history. If, by the age of 20, such long-term effects are found, these could persist into middle and late adult life and contribute to the evolution of chronic respiratory disease.

Opportunities for the prevention of serious respiratory disease in infancy and childhood are few. If parents who smoke give up the habit they can reasonably expect to lose, or at least experience an improvement in their respiratory symptoms. This might well result in reduction of respiratory illnesses in their children. At the same time the absence of cigarette smoke in the home could be expected to diminish the risk of attacks of pneumonia and bronchitis in their children during the first year of life.

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"The atomic physicists were as clever, as modest, as self-seeking, as mean, as argumentative and just as concerned for humanity as the microbe hunters. The physicists worked to produce a weapon of war, but there is no real evidence that the nationalistic arguments which convinced them that their efforts were right and just were any different from those that so affected Koch and Pasteur half a century earlier; and the intellectual challenge was just as great, and grappling with it just as enjoyable. . . . The physicists' work was widely seen as being culpable because it was applied to the taking of life; the first two atomic bombs did so on a vast and horrifying scale. But it was Pasteur, and not some atomic physicist, who in 1870 said of the Germans, ' I want to see the war prolonged into the depths of winter, so that all those vandals confronting us shall perish of cold and hunger and disease '."—ROBERT REID, Microbes and Men; p. 168. London: B.B.C. Publications. 1974. £2.50.

Colley, J.R.T., Holland, W.W., Corkhill, R.T. "Influence of Passive
Smoking and Parental Phlegm on Pneumonia and Bronchitis in Early
Childhood" The Lancet (November 2): 1031-1034, 1974.

SUMMARY: The incidence of pneumonia and bronchitis has been studied
in 2205 infants over the first five years of life. In the same
period their parents' smoking habits and respiratory symptoms were
recorded annually. The incidence of pneumonia and bronchitis in
the first year of life was associated with parents' smoking habits;
incidence was lowest where both parents were non-smokers, highest
where both smoked, and lay between these two levels where only one
parent smoked. Over the age of one year the association was not
consistent. When parents' respiratory symptoms were also studied
a close association was found with the incidence of pneumonia and
bronchitis in the child; this was independent of parents' smoking
habits and was an almost consistent finding throughout the first
five years of life. In the first year of life exposure to cigarette
smoke generated when parents smoked doubled the risk for the infant
of an attack of pneumonia or bronchitis.

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2023382719

Lebowitz, M.D., Burrows, B. "Respiratory Symptoms Related to Smoking Habits of Family Adults" Chest 69(1):48-50, 1976.

ABSTRACT: A study of the effects of family smoking habits on the symptoms of other family members has shown that symptoms of household members, especially children, are related to smoking habits within the households but are not significantly so when symptoms in adults are controlled.

2023382720

Respiratory Symptoms Related to Smoking Habits of Family Adults*

Michael D. Lebowitz, Ph.D.; and Benjamin Burrows, M.D., F.C.C.P.

A study of the effects of family smoking habits on the symptoms of other family members has shown that symptoms of household members, especially children, are re- lated to smoking habits within the households but are not significantly so when symptoms in adults are controlled.

It has been suggested that smoking habits of indi- viduals in a family may have an effect on the health of other family members, particularly chil- dren, through environmental exposure to tobacco smoke.[1,4] Colley[1] has demonstrated such an effect, and Holland[2] (personal communication, August, 1974) has also inferred the possibility that such an effect exists. But, as noted by Colley[1] and others,[2,3] the data are complicated by concurrent relation- ships of children's symptoms to other familial fac- tors, particularly the relation of children's symptom reports to parents' symptom reports, and it remains uncertain that parental smoking habits per se are related to symptoms in children.

This report examines the question of the effect of cigarette smoking in the household on household members. Personal smoking habits within age group, as well as parental symptom histories, are examined in this relationship. Children's symptoms are emphasized, and other important factors, such as social status and family size, are examined.

METHODS

The Tucson Epidemiological Study of Obstructive Lung Diseases is a longitudinal study of a stratified cluster random sample of Anglo-white households in the community. Meth- ods of study have been described in detail elsewhere.[4] The final sample consisted of 3,484 Anglo-white individuals from a total 1,655 households. Each individual within the house- hold completed a self-administered questionnaire, which con- tained information on demographic characteristics, medical history, respiratory history, migration, smoking, and other factors possibly associated with obstructive pulmonary dis- eases. Respiratory symptom questions included those in the

National Heart and Lung Institute Standardized Respiratory Symptom Questionnaire, a modification of the British Med- ical Research Council Respiratory Questionnaire. For subjects under age 15, the questionnaire was completed by the parent or guardian. Social and environmental histories, occupational histories on those employed, and family histories were ob- tained by trained nurse-interviewers. Objective tests per- formed included flow-volume measurements.

This paper is concerned with the symptoms of persistent cough, persistent phlegm, wheeze, physician-confirmed asthma or bronchial trouble, emphysema, and others.

Socioeconomic status was represented by the socioeconomic strata used in the initial selection of the population, by the head-of-household's education, and by family income. Each family's smoking and symptom histories were derived from the adult information.

Tabular analysis of data was performed, with all data processing being performed on a computer (CDC 6400). Parametric and nonparametric tests of significance were utilized.

Children under 15 years were presumed to be nonsmokers. Of the sixty 14-year-old children completing smoking his- tories, only two girls indicated any smoking history, and they smoked very few cigarettes.

RESULTS

Children in households with present smokers have higher overall rates of persistent cough, persistent phlegm, wheezing on most days, and physician- confirmed asthma, bronchial trouble, or emphy- sema" than those children in households with only ex-smokers or those who never smoked, as seen in Table 1. Although the trend exists for all of the conditions, only the trend for persistent cough was statistically significant. The results for all adult non- smokers are also seen in Table 1. There was no significant trend in adult symptoms in relation to household smoking. There were no significant age differences in symptom prevalence rates in adult nonsmokers.

Further analyses were performed to determine if the effect observed in children might result from

Table 1—*Prevalence Rates of Symptoms by Smoking History in the Household. Controlling for Individual Smoking History and Age*

Age and Individual Smoking Group by Household (HH) Smoking Habits	Prevalence Rate (per 100)				
	Persistent Cough	Persistent Phlegm	Wheezing Most Days	Physician-Confirmed ABE*	No.
Children (<15 yr)					
HH: Present smokers	10.4	5.9	3.9	21.7	337
Ex-smokers	3.7	3.7	1.8	16.6	163
Never smokers	6.3	2.4	0.8	17.5	126
Total	7.8	4.6	2.8	19.5	626
P (X²)**	<0.05	NS	NS	NS	....
Never smokers (+15 yr)†					
HH: Present smokers	6.8	8.6	4.5	17.6	267
Ex-smokers	8.1	6.5	5.5	22.6	309
Never smokers	10.3	8.6	4.4	18.9	682
Total	9.0	8.1	4.7	19.5	1,258
P (X²)**	NS	NS	NS	NS	

*Asthma, bronchial trouble, or emphysema

**NS, Not significant

†Rates not significantly age-dependent in adults who never smoked

differences in ages of children, social status, family size, or migration status in households of different smoking habits. These factors did not significantly differ between such households.

The prevalence rates of children's symptoms were examined in relationship to both current smoking habits and symptom histories of adults in the household (Table 2). Children in households containing adults with the specific symptoms had a higher prevalence of symptoms, regardless of the family smoking habits. When the presence of symptoms in adults was taken into account by partitioning households into those where adults had the symptom(s) and those where adults didn't have the symptom(s),

no statistically significant difference remained in children's symptoms related to the household smoking habits. However, though not statistically significant, most children's symptoms were consistently higher in currently smoking families than in currently nonsmoking families.

Some prevalence rates of children's symptoms within presently smoking households with adult symptoms were significantly greater than symptom rates for children in the households without symptoms in adults.

There were no significant differences in children's prevalence rates of bronchiolitis, croup, pneumonia, or a combination of those three, in relation to the

Table 2—*Prevalence Rates of Children's Symptoms in Relation to Their Household's Adults' Smoking Habits and Symptoms*

Household Smoking and Symptoms	Prevalence and Prevalence Rates (per 100) of Children's Symptoms											
	Persistent Cough		Persistent Phlegm		Persistent Cough and/or Phlegm		Wheeze		Physician-Confirmed ABE*		All Respiratory Symptoms**	
	No.	Rate	No.	Rate	No.	Rate	No.	Rate	No.	Rate	No.	Rate
Households with symptoms												
Present smokers	29	16.9†	21	12.8†	40	20.0	115	43.7†	41	27.3	173	50.1
Ex- and never smokers	4	13.8	3	10.0	6	13.0	50	44.7	25	23.4	99	44.8
Households without symptoms												
Present smokers	16	7.2	6	2.6	13	6.6	22	24.1	47	19.3	20	39.2
Ex- and never smokers	11	3.7	6	2.0	11	3.9	46	23.4	28	12.6	28	25.9

*Asthma, bronchial trouble, or emphysema.

**All of preceding symptoms and exertional dyspnea (grade 2+); unconfirmed ABE; and physician-confirmed emphysema, chronic bronchitis, bronchiectasis, and/or asthma.

†Significantly higher (P<0.05) than rate for children in households without symptoms (any smoking category), but not higher than ex- or never smokers in households with symptoms, as per tests of difference between proportions and chi-square.

smoking habits of either or both parents. No differences in findings were noted if one examined symptoms by whether the father alone, the mother alone, or both smoked.

Symptoms in children and in families were related to one another. When all the combinations of children's symptoms were examined in relation to adult household smoking and symptoms, the trends were almost always the same as previously found, though not statistically significant.

Discussion

The results from this study do not indicate the same significance of social status, family size, or specific age of children in relation to the effect of household smoking on children's symptoms that Colley[1] found, but they do confirm that symptoms within the adults of the household definitely appear to influence the symptoms reported for the children.

This finding has far-reaching significant ramifications related to both the reporting of symptoms in children and factors which may be responsible for such familial aggregation of symptoms. Longitudinal follow-up of the children in the various types of households may help detect any long-term effect of paternal smoking.

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ANNOUNCEMENT

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2023382724

Leeder, S.R., Corkhill, R., Irwig, L.M., Holland, W.W., Colley,
J.R.T. "Influence of family factors on the incidence of lower
respiratory illness during the first year of life" Brit. J. prev.
soc. Med. 30: 203-212, 1976.

SUMMARY: In a study of a cohort of over 2000 children born between
1963 and 1965, the incidence of bronchitis and pneumonia during
their first year of life was found to be associated with several
family factors. The most important determinant of respiratory
illness in these infants was an attack of bronchitis or pneumonia
in a sibling. The age of these siblings, and their number, also
contributed to this incidence. Parental respiratory symptoms,
including persistent cough and phlegm, and asthma or wheezing, as
well as parental smoking habits, had lesser but nevertheless
important effects. Parental smoking, however, stands out from all
other factors as the one most amenable to change in seeking to
prevent bronchitis and pneumonia in infants.

Influence of family factors on the incidence of lower respiratory illness during the first year of life

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Leeder, S. R., Corkhill, R., Irwig, L. M., Holland, W. W., and Colley, J. R. T. (1976). *British Journal of Preventive and Social Medicine*, **30**, 203-212. Influence of family factors on the incidence of lower respiratory illness during the first year of life. In a study of a cohort of over 2000 children born between 1963 and 1965, the incidence of bronchitis and pneumonia during their first year of life was found to be associated with several family factors. The most important determinant of respiratory illness in these infants was an attack of bronchitis or pneumonia in a sibling. The age of these siblings, and their number, also contributed to this incidence. Parental respiratory symptoms, including persistent cough and phlegm, and asthma or wheezing, as well as parental smoking habits, had lesser but nevertheless important effects. Parental smoking, however, stands out from all other factors as the one most amenable to change in seeking to prevent bronchitis and pneumonia in infants.

This paper and the two that follow concern family factors that influence the incidence of respiratory illness and development of ventilatory function in children during the first five years of life.

Respiratory illnesses remain a major cause of death in infancy; the mortality rate for these diseases in infants in England and Wales has changed little since 1955 despite many new antibiotics. Viruses and allergies, rather than bacteria, are probably now responsible for many of the more serious respiratory illnesses in infancy (Colley, 1971; Glezen and Denny, 1973). As the management of viral and allergic illness is often difficult, there is good reason to seek ways in which these illnesses may be prevented. Prevention could also have other, long-term, benefits. Although clinical recovery from acute respiratory illness in childhood is usual, it may not always be as complete as has been assumed. In a number of studies, children with a history of lower respiratory tract illness have been found to have lower ventilatory function than children who escaped such illnesses (Wahdan, 1963; Lunn,

Knowelden, and Handyside, 1967; Holland *et al.*, 1969a; Colley and Reid, 1970; Bland, Holland, and Elliott, 1974). In a birth cohort followed-up until the age of 20 years, Colley, Douglas, and Reid (1973) found that those with a history of lower respiratory tract illness when under two years of age had a higher prevalence of respiratory symptoms at the age of 20 than those without this history. These findings are interpreted as evidence for some degree of permanent lung damage after childhood respiratory illness. Thus, prevention of acute lower respiratory illness in childhood may help to reduce respiratory morbidity in adult life.

Prevention of lower respiratory illness in infancy may be achieved in several ways. The opportunity for infection can be reduced by decreasing susceptibility through immunization, and by limiting contact of infants with others suffering from these illnesses. Complications may be reduced by more effective management of acute illness. However, the most promising current approach must involve the modification of factors that are known to increase the risk of these illnesses. Parental smoking has been identified as one such factor (Colley, Holland, and Corkhill, 1974). While other factors have been identified as contributing

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to the incidence of respiratory disease in children, changes in them will often involve major environmental manipulation which may not be feasible. By contrast, parental smoking is potentially modifiable. Children of parents who smoke in the home have been found to have an increased risk of bronchitis and pneumonia in comparison with children of non-smoking parents. This is, in part, attributable to passive inhalation by infants of their parents' cigarette smoke.

In this paper we investigated a number of family factors to find out their influence on lower respiratory illness during the first year of life. In the next paper, factors influencing the incidence of wheezing and asthma during the first five years are considered. In the third paper, family factors influencing ventilatory function at the age of five years are examined.

METHODS

The methods described in this section apply to the following two papers also.

STUDY SAMPLE

A cohort of children born between 1963 and 1965 in Harrow, a residential suburb of north-west London, was followed-up for the first five years of life together with other members of their families. The sampling methods have been described (Colley and Holland, 1967; Holland et al., 1969b; Colley et al., 1974). All families living in six wards of the borough of Harrow who had an infant born to them between 1 July 1963 and 30 June 1965 were included in the study population, the only exclusions being families of infants who died within seven days of birth. A total of 2365 Harrow families were eligible for our study. However, of these

2365 families, 160 could not be visited or declined to participate, leaving 2205 (93%) for investigation (Table 1). The families were followed-up annually for five years, although it was not possible to assemble complete data on all individuals on all occasions. In the tables presented in this paper, the number of subjects available for study is specified in footnotes and set out in detail in Table 1.

ENROLMENT PROCEDURES

Health visitors, specially trained as observers for our study, visited infant (subsequently referred to as the index child) and mother at home within 14 days of the infant's birth, administered a questionnaire to the parents, and measured the child's crown-rump length and chest circumference. The questionnaire sought among other items the birth weight of the infant and details of health at birth. A one-in-three systematic sample of families was then visited by a field team from St Thomas's Hospital. The field team readministered the questionnaire used by the health visitors and repeated the body measurements.

MEASUREMENT OF VENTILATORY FUNCTION

In addition to readministering the questionnaire, the field team measured the ventilatory capacity of the infant using a portable pneumotacograph (Colley, 1965). Parents and other children in the family also had measurements of peak expiratory flow rates made, using the low-range Wright peak flow meter for the children and the adult range meter for the adults. All recordings using the peak flow meter were made with the subject seated. Five peak expiratory flow manoeuvres were recorded

TABLE 1
HARROW STUDY POPULATION: NUMBERS OF INFANTS, MOTHERS, FATHERS, SIBLINGS, AND PARENT PAIRS BY YEAR OF STUDY

Year of Study	Infants	Infants with Lung Function	Mothers	Fathers	Siblings	Infant and Parent Pairs	Parent Pairs
Initial interview	2149	543	2148	2130	2051	—	2129†
Follow-ups:							
First year	2122*	551	2120	2079	1959*	2077†	2077†
Second year	2109	396	2103	2052	1929	2048	2048
Third year	2096	484	2092	2036	1890	2032	2032
Fourth year	2097	475	2074	1993	1819	1970	1970
Fifth year	2095	459	2086	1998	1822	1969	1969
From initial to fifth year follow-up	2044	—	2010	1906	—	1875	1875
From first year to fifth year follow-up	2044	—	2011	1908	—	1875	1875

*Families with an infant and at least one sibling at first year follow-up—1170.
†Infants at the first year follow-up with parent pairs over initial and first year follow-up—2074.

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for each subject, the mean of the last three being used for analysis. The families in the one-in-three systematic sample were visited annually by members of the field team. Measurements of ventilatory function were made each year. Satisfactory records were not obtained from all subjects each year. Numbers of subjects with satisfactory records for analysis in the various tables are given in Table 1, and elsewhere are indicated as footnotes. A comparison of the age, sex, and social class characteristics of these children and adults for whom ventilatory function data were available with those of the entire study sample revealed no important differences.

A total of 623 infants were eligible for measurement of lung function initially, of whom 487 had satisfactory records for all the five years. Measurements of ventilatory function were obtained in 460 mothers and 427 fathers when their children were aged five years.

RESPIRATORY SYMPTOMS AND ILLNESSES

At the initial interview the health visitor also obtained information concerning parents' smoking habits and respiratory symptoms.

Positive responses from parents to the question 'Do you usually cough first thing in the morning in the winter?' and/or 'Do you usually bring up phlegm from your chest first thing in the morning in winter?' were regarded as evidence of respiratory disability subsequently referred to as 'cough-phlegm'. Positive responses to the questions 'Does your chest ever sound wheezy or whistling?' and/or 'Have you ever had asthma?' were also regarded as evidence of respiratory disability termed 'asthma-wheeze'. At the initial examination and at the end of the first year of follow-up, parents were asked, 'Do you smoke?'. They were classified as smokers if they reported smoking

both at the initial examination and at the end of the first year of follow-up, as non-smokers if they were smoking on neither occasion, and otherwise as changed smokers, see Table II. The validity of answers to these questions has already been established (Holland *et al.*, 1969a). Social class was derived from the father's occupation using the Registrar General's classification (General Register Office Classification of Occupations, 1960).

FOLLOW-UP

The families were followed-up annually for five years; the one-in-three sample was interviewed at the end of each year and the rest were followed-up with postal questionnaires. Information about the health of the family during the previous 12 months and on changes in parental occupation and smoking habits was obtained each year. If the father changed his occupation, social class for the year in which the change occurred was derived from his occupation at the beginning of that year. Parents were also asked about cough-phlegm and bronchitis or pneumonia in the siblings of index infants and in the index infants themselves using the questions, 'Has he or she had, in the past 12 months, bronchitis? pneumonia? bad colds? whooping cough?'. The parents' accounts of these illnesses were checked, in a sample, by examining general practitioners' records and the level of agreement between the parental and medical data was adequate (Colley, *et al.*, 1974). At the end of the third and subsequent years, parents were asked of their children, 'Has he or she ever had asthma?' and 'Does his or her chest ever sound "wheezy", "chesty" or "whistling"?'. In the fourth and fifth years this question was modified by the parenthesis, 'other than when he or she has a cold'. Parents were also asked to name all illnesses they could recall their child having suffered during the

TABLE II
DEFINITION OF CATEGORIES USED TO TABULATE PARENTAL SMOKING HABITS

		Parental Smoking Habit			
		Mother		Father	
		At Initial Interview	At First Annual Follow-Up	At Initial Interview	At First Annual Follow-Up
Parental smoking category used in Tables III and IV	Neither	−	−	−	−
	One A:	+	+	−	−
	B:	−	−	+	+
	Both	+	+	+	+
	Habit changed	All other combinations			

− = Not smoking   + = Smoking   A and B are alternatives (i.e. either mother, or father is a regular smoker)

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previous year, whether these had led to hospital admission, medical consultation, or no action.

Parents were also asked each year about cough-phlegm which they may have suffered themselves during the previous 12 months. In the following analyses, the influence of parental cough-phlegm on respiratory illness in children has been studied over different periods. Children were classified according to prevalence of parental cough-phlegm reported at the end of the first year of life of the index child, see Tables IV, V, and VIII. In Table X children were classified according to parental cough-phlegm prevalence at both the beginning and end of the first year. Consequently the number of children whose parents had no cough-phlegm in this classification was less (1286) than if prevalence of cough-phlegm at the end of the first year was considered alone (1498).

In the next paper 'Influence of family factors on asthma and wheezing during the first five years of life' (pages 213-218), parental cough-phlegm was considered during the full five-year period and not simply in the first year. The effect of change in parental cough-phlegm prevalence during these five years was also studied. Consequently, in Tables IV and V of that paper, parental cough-phlegm refers to the entire five-year period. The numbers in all these tables are further modified by availability of data for other classification variables (such as parental smoking habits in Table IV of this paper) as explained in the footnotes to the tables.

RESULTS

During the first year of life, the incidence of bronchitis and pneumonia varied according to several family factors. These illnesses occurred much more commonly in infants born to families which had several other children already, and in those families where the parents had respiratory disability or were smokers.

Children whose parents both had a history of asthma-wheeze had an incidence of bronchitis or pneumonia of 26·9% which was three times greater than that found in children of parents without such a history (9·4%) (Table III). The effect of parental smoking was not so great. The incidence of bronchitis or pneumonia in children of non-smoking parents was 7·2% compared with 17·7% when both parents smoked. When both smoking habits and asthma-wheeze were examined for combined effects on the incidence of bronchitis or pneumonia in the children, these contrasts widened. For example, the incidence of bronchitis or pneumonia was 6·7% in infants whose parents neither smoked nor had suffered from asthma-wheeze; this contrasted with an incidence of 39·3% when both parents smoked and had a history of asthma-wheeze.

Parental cough-phlegm, like asthma-wheeze, was associated with a higher incidence of bronchitis or pneumonia in the children (Table IV). Children whose parents did not give this history had an incidence of bronchitis or pneumonia of 9·5% compared with 26·3% of those whose parents both had this symptom. However these associations while strong, were not wholly consistent. Incidence of bronchitis or pneumonia did not always increase in line with presence of symptoms in parents, as seen in the case of the combined influence of these symptoms and parental smoking habits. This may in part be a consequence of these rates being based upon small numbers.

TABLE III

ANNUAL INCIDENCE PER 100 INFANTS OF BRONCHITIS OR PNEUMONIA IN THE FIRST YEAR OF LIFE BY PARENTAL HISTORY OF ASTHMA-WHEEZE AND SMOKING HABIT

		Parental Smoking Habit				
		Neither	One	Both	Habit Changed	Total
Parental asthma-wheeze	Neither	6·7 (451)	9·6 (502)	13·7 (314)	8·7 (241)	9·4 (1508)
	One	8·9 (101)	18·0 (178)	22·3 (139)	7·4 (81)	15·6 (499)
	Both	14·3 (7)	13·6 (22)	39·3 (28)	30·0 (10)	26·9 (67)
	Total	7·2 (559)	11·8 (702)	17·7 (481)	9·0 (332)	11·5 (2074)*

Populations in parentheses
*Total excludes 27 infants with missing first year data and an additional 48 with missing initial and first year data on parent pairs.

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TABLE IV

ANNUAL INCIDENCE PER 100 INFANTS OF BRONCHITIS OR PNEUMONIA IN THE FIRST YEAR OF LIFE BY PARENTAL HISTORY OF COUGH-PHLEGM AND SMOKING HABIT

		Parental Smoking Habit				
		Neither	One	Both	Habit Changed	Total
Parental cough-phlegm	Neither	7·6 (490)	10·8 (474)	13·8 (290)	6·2 (244)	9·5 (1498)
	One	3·3 (61)	10·1 (199)	25·4 (142)	15·2 (79)	14·6 (481)
	Both	12·5 (8)	14·4 (29)	18·4 (49)	33·3 (9)	26·3 (95)
	Total	7·2 (559)	11·8 (702)	17·7 (481)	9·0 (332)	11·5 (2074)*

Populations in parentheses
*Total excludes 27 infants with missing first year data and an additional 48 with missing initial and first year data on parent pairs.

TABLE V

ANNUAL INCIDENCE PER 100 INFANTS OF BRONCHITIS OR PNEUMONIA IN THE FIRST YEAR OF LIFE BY PARENTAL HISTORY OF COUGH-PHLEGM AND ASTHMA-WHEEZE

		Parental Cough-Phlegm			
		Neither	One	Both	Total
Parental asthma-wheeze	Neither	8·7 (1174)	10·4 (288)	21·7 (46)	9·4 (1508)
	One	12·1 (298)	19·4 (365)	27·8 (36)	15·6 (499)
	Both	19·2 (26)	28·6 (28)	38·5 (13)	26·9 (67)
	Total	9·5 (1498)	14·6 (481)	26·3 (95)	11·5 (2074)*

Populations in parentheses
*Total excludes 27 infants with missing first year data and an additional 48 with missing initial and first year data on parent pairs.

TABLE VI

ANNUAL INCIDENCE PER 100 INFANTS OF BRONCHITIS OR PNEUMONIA IN THE FIRST YEAR OF LIFE BY NUMBER OF SIBLINGS AND THEIR HISTORY OF BRONCHITIS OR PNEUMONIA DURING THAT YEAR

		Number of Siblings				
		0	1	2	3 or More	Total
Bronchitis or pneumonia in siblings during first year of life of index infants	None	7·4 (925)	10·0 (641)	12·3 (268)	17·8 (146)	9·8 (1980)
	One or more episodes	—	40·7 (54)	37·0 (27)	35·3 (34)	38·2 (115)
	Total	7·4 (925)	12·4 (695)	14·6 (295)	21·1 (180)	11·4 (2095)*

Populations in parentheses
*Total excludes 27 infants with missing first year data; and 27 with siblings for whom first year data were missing.

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Children of parents with a history of both asthma-wheeze and cough-phlegm had a higher incidence of bronchitis and pneumonia in the first year than did children whose parents had one or other but not both of these symptoms (Table V).

The incidence of bronchitis and pneumonia in the index infants was closely associated with both the number of siblings in the family and their respiratory history (Table VI). The most important items of respiratory history were attacks of bronchitis or pneumonia in a sibling during the first year of life of the index infant. When this occurred the overall incidence was 38·2%. This contrasted with an incidence of 7·4% in the 925 infants who had no siblings.

There was also an association between the age of the siblings and incidence of bronchitis and pneumonia in the index infants. This was most obvious in relation to the eldest sibling—that is, the first child in each family, as shown in the top row of Table VII. There was a steady increase in incidence of illness with increasing age of the eldest sibling, being lowest when the eldest sibling was under three years and highest when the eldest sibling was aged five, and thus likely to be starting school. If the eldest sibling was over five years old the trend with age reversed; the incidence of illness in index infants was lower the older the sibling. When all siblings were considered together irrespective of their position in the family (bottom row Table VII), a similar relationship was found between mean age and incidence of illness in the index infants.

Factors such as ambient air pollution and low socioeconomic class have been shown to be important in the development of respiratory symptoms and illnesses in other groups of children (Holland *et al.*, 1969b; Colley and Reid, 1970).

However, no variation in illness incidence was found in the children in this study during the first year of life which could be attributed to the influence of social and physical environmental factors. The different areas in which the children lived showed little variation in general environment and air pollution at the time the index children were born, although there had been differences in pollution levels not many years before. This previous difference may explain the variation found in the incidence of respiratory illness among the older siblings in this sample (Colley and Holland, 1967) living in different areas of Harrow.

Bronchitis and pneumonia in the siblings was also associated with a history of cough-phlegm in the parents as seen in Table VIII. This association was independent of family size, and was present in families with one, two, three, or more siblings. A similar relationship was found between sibling bronchitis and pneumonia and parental asthma-wheeze (Table IX).

Examination of the data thus far presented did not suggest any multiplicative interaction between the various factors associated with bronchitis and pneumonia in the index infants. However, because some of the factors were themselves interrelated (for example, parental cough-phlegm and smoking), it was difficult to assess the influence of each individual factor upon the incidence of respiratory illness in the children. By fitting a logistic model to the data, with the incidence of bronchitis and pneumonia in the index children as the outcome variable, this aspect was investigated further. The independent variables included in the model were parental smoking, parental cough-phlegm (considered at several levels depending upon its presence in parents at both the beginning

TABLE VII

ANNUAL INCIDENCE PER 100 INFANTS OF BRONCHITIS OR PNEUMONIA DURING THE FIRST YEAR OF LIFE BY AGE (YEARS) OF SIBLINGS AND THEIR POSITION IN THE FAMILY

		Age of Eldest Sibling at the End of the First Year of Life of Index Infant					
		Under 3	3	4	5	6 or More	Total
Position of sibling (counting from eldest)	First	9·5 (201)	10·8 (251)	13·2 (182)	23·2 (108)	17·1 (434)	14·4 (1176)
	Second	9·5 (74)	17·3 (81)	25·0 (72)	18·2 (55)	16·5 (200)	17·0 (482)
	Third and younger	21·1 (57)	19·1 (42)	16·7 (36)	32·2 (28)	27·0 (137)	24·0 (300)
	All siblings	11·5 (332)	13·1 (374)	16·6 (290)	23·1 (191)	18·7 (771)	16·5 (1958)*

Populations in parentheses
*Total consists of the number of siblings with first year data. The total number of siblings in the study was 2051. Details of the number of infants included in the table (subtotal for the first row) are given in Table VI. An additional six infants are included in this table for whom data were available for their eldest (if not all other) siblings.

TABLE VIII

ANNUAL INCIDENCE PER 100 FAMILIES OF BRONCHITIS OR PNEUMONIA IN ANY SIBLINGS OF THE INDEX INFANTS BY NUMBER OF SIBLINGS AND PARENTAL HISTORY OF COUGH-PHLEGM

		Number of Siblings			
		1	2	3 or More	Total
Parental cough-phlegm	Neither	6.7 (492)	7.8 (192)	16.3 (98)	8.2 (782)
	One	10.1 (158)	11.4 (79)	17.5 (63)	12.0 (300)
	Both	17.2 (29)	13.0 (23)	43.8 (16)	22.1 (68)
	Total	8.0 (679)	9.2 (294)	19.2 (177)	10.0 (1150)*

Populations in parentheses
*Total excludes 27 infants with missing first year data; 925 infants with first year data available but who had no siblings; 27 with a sibling but for whom first year data were missing; and 20 families with missing first year data on parent pairs.

TABLE IX

ANNUAL INCIDENCE PER 100 FAMILIES OF BRONCHITIS OR PNEUMONIA IN ANY SIBLINGS OF THE INDEX INFANTS BY NUMBER OF SIBLINGS AND PARENTAL HISTORY OF ASTHMA-WHEEZE

		Number of Siblings			
		1	2	3 or More	Total
Parental asthma-wheeze	Neither	7.9 (518)	7.7 (195)	13.5 (119)	8.7 (832)
	One	6.4 (156)	10.2 (88)	29.4 (51)	11.5 (295)
	Both	18.8 (16)	27.3 (11)	33.3 (9)	25.0 (36)
	Total	7.8 (690)	9.2 (294)	19.0 (179)	9.9 (1163)*

Populations in parentheses
*Total excludes 27 infants with missing first year data; 925 infants with first year data available but who had no siblings; 27 with a sibling but for whom first year data were missing; and seven families with missing initial data on parent pairs.

and the end of the first year), parental asthma-wheeze, number of siblings, sibling bronchitis or pneumonia, sibling cough-phlegm, sex of child, social class of father, and areas of residence. Several factors, notably social class, residential area, and sibling cough-phlegm made no significant contribution to the model which was then refitted without these variables. The results from this second model are presented in Table X. Bronchitis and pneumonia in siblings was found to have the largest effect upon the adjusted incidence rates of bronchitis and pneumonia in the index infants; the adjusted incidence rate was 8.6% in the absence of this factor and 47.6% when two or more siblings had these illnesses. Parental smoking had the next largest effect and parental asthma-wheeze had a lesser, but significant, effect in the model.

Crude incidence rates suggested a strong relationship between parental cough-phlegm and illness in the index infants. The influence of parental cough-phlegm was strongest when parents reported that they had suffered from cough-phlegm both at the time of the initial interview and when interviewed again one year later. Thus among children of parents who reported cough-phlegm on the two occasions, 42.1% (that is eight out of 19) suffered from bronchitis or pneumonia compared with only 9.0% (that is, 116 out of 1286) in children whose parents were free of cough-phlegm initially and at the end of the first year. However, when adjustment had been made for other factors in the model, the effect of parental cough-phlegm was no longer statistically significant.

TABLE X

CRUDE AND ADJUSTED INCIDENCE RATES PER 100 INFANTS FOR BRONCHITIS OR PNEUMONIA FOR LEVELS OF EACH FACTOR WITH ESTIMATES OF THEIR EFFECTS

Factor and Level	Crude Incidence Rate	Adjusted Incidence Rate	Significance of the Factor in the Model		
			x^2	df	P
Parental smoking					
Neither smoke	6·7 (553)	6·2	24·11	3	P < 0·0005
Changed habit	8·9 (327)	7·7			
One smokes	11·6 (695)	9·7			
Both smoke	17·5 (473)	15·4			
Parental cough-phlegm					
A*	9·0 (1286)	8·9	6·50	4	0·1 < P < 0·2
B	13·1 (396)	10·2			
C	12·8 (281)	8·3			
D	28·1 (64)	16·5			
E	42·1 (19)	16·7			
Parental asthma-wheeze					
Neither	9·2 (1494)	8·3	8·60	2	0·01 < P < 0·025
One	15·2 (488)	11·8			
Both	27·3 (66)	16·5			
Sex of child					
Male	12·9 (1088)	11·1	8·14	1	0·001 < P < 0·005
Female	9·4 (960)	7·5			
Number of siblings					
None	7·3 (900)	7·2	11·08	2	0·001 < P < 0·005
One	12·2 (678)	10·5			
Two or more	17·2 (470)	12·6			
Bronchitis or pneumonia in siblings					
No attacks†	9·6 (1933)	8·6	39·83	2	P < 0·0005
One sibling with illness	35·3 (102)	27·0			
Two or more siblings with illness	61·5 (13)	47·6			
Total	11·2 (2048)‡				

*A—neither parent ever had cough-phlegm: B—one parent had it either at the beginning or end of the first year of life of index child:
C—both parents had it once or one parent had it twice;   D—one parent had it once, and the other twice: E—both parents had it twice.
†i.e. either no siblings, or if siblings, then they had no illness.
‡Total excludes 27 families with infants with missing first year data; an additional 27 families with siblings with missing first year data, and 47 families with missing initial or first year data on parent pairs.
Populations in parentheses

There was a sex difference in the incidence of bronchitis and pneumonia in the children; the adjusted overall incidence for boys being 11·1% compared with 7·5% for girls.

To determine whether these factors were specifically related only to a history of lower respiratory illness in the index infants their association with upper respiratory illnesses was also examined using a logistic model. Here the outcome variable was the incidence of 'bad colds' in the first year. In this model, only parental cough-phlegm and sibling bronchitis or pneumonia were statistically significant factors (P < 0·001 in each case) but parental smoking and asthma-wheeze were not. The overall association between bad colds and these family factors was considerably weaker than was their association with bronchitis or pneumonia.

Discussion

The present study has been concerned with attempting to identify and separate the various family factors influencing the incidence of acute lower respiratory illness in children during their first year of life. Colley et al. (1974) have already shown that both smoking and phlegm production by parents contribute to the incidence of respiratory disease in these children. This paper extends the investigation and demonstrates the additional influence of a parental history of asthma-wheeze, and the importance of both the number of siblings and their history of respiratory disease.

Parental asthma-wheeze was found to be associated with respiratory illness in the index infants in a different way to that seen for parental cough-phlegm. Parental asthma-wheeze appears to exert its influence independent of the number, age, or respiratory illness history of the siblings. This contrasted with parental cough-phlegm, where these factors did appear to have an influence both on infant respiratory illness and the parental symptoms themselves.

A further difference between the effects of parental cough-phlegm and asthma-wheeze was apparent when the incidence of bad colds was

examined in relation to the factors shown to be important in the incidence of bronchitis and pneumonia. Parental cough-phlegm was associated with an increased risk of bad colds in the index infants, whereas parental asthma-wheeze was without effect. Taken together these observations suggest that genetic factors may be more important in explaining the association between parental asthma-wheeze and bronchitis and pneumonia in the children than they are in the case of parental cough-phlegm. Here an environmental factor which is intimately related to parental smoking habits and sibling respiratory illness history is probably implicated.

Sibling bronchitis or pneumonia, parental cough-phlegm, parental asthma-wheeze and bronchitis or pneumonia in the index infants were all closely associated in this study. The analysis using a logistic model suggested that sibling illness had the greatest effect although this must be interpreted within the limitations implicit in the use of the model. Without further information about the time sequence of illness in parents, siblings, and index infants it is not possible to decide exactly how cause and effect should be imputed in this situation. The finding that sibling illness appeared to be the most important factor is consistent with other family studies where siblings have been found to serve as primary cases in family epidemics of respiratory illness (Brimblecombe *et al.*, 1958; Dingle, 1973; Williams, 1975). That the association between sibling illnesses and illness in the index infants was strongest when the siblings were of school starting age makes cross-infection from the siblings a likely circumstance as this age is known to be one of high incidence of respiratory illness (Reid, 1969).

The association of parental asthma-wheeze with bronchitis and pneumonia in the first year of life raises the possibility that some episodes of 'bronchitis' or 'pneumonia' were really episodes of asthma. We examined this question by noting the subsequent course of children with respect to asthma at ages three, four, and five years. Some children of parents with asthma-wheeze subsequently developed asthma themselves. Other children of parents with the same history did not develop asthma. These two groups of children had a similar incidence of bronchitis and pneumonia in the first year of life. Assuming equal exposure and susceptibility to respiratory pathogens in these two groups of children (that is those who subsequently developed asthma and those who did not), there is thus no evidence in this study to suggest that

parents with asthma-wheeze tended to call asthmatic attacks in their children 'bronchitis' or 'pneumonia'.

In this study, cigarette smoking by parents stands out from all the other factors associated with bronchitis and pneumonia in young children, as the one most amenable to change. There seems to be good reason for actively bringing to the notice of smoking parents the dangers this habit carries for their young children.

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ABSTRACT. A portable personal air pollution sampler was used to measure the exposure of twenty children to respirable particulates, sulfur dioxide, and nitrogen dioxide over a 24-hour period. Particulate exposures were significantly higher among children who lived with one or more smokers, and exceeded the primary air quality standard in nineteen of the twenty subjects. To a large extent, an individual's respirable particulate load appears to be determined by exposure to indoor rather than outdoor pollutants.

Importance of the Indoor Environment in Air Pollution Exposure

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ABSTRACT

A portable air pollution sampler was used to measure the exposure of twenty children to respirable particulates, sulfur dioxide, and nitrogen dioxide over a 24-hour period. Personal exposures were significantly higher among children who lived with cigarette smokers, and exceeded the primary air quality standard for respirable particulates had applied to the indoor environment.

AIR POLLUTION STUDIES of children have been of particular interest because children constitute a nonsmoking, nonoccupationally-exposed group who have generally lived in one community for most of their lives. To date, such investigations have concentrated on outdoor air pollution. However, children bring in a temperate region spend from 60% to 80% of their time indoors on an average school day. We therefore decided to monitor the 24-hour period to determine the importance of the indoor environment as a determinant of an individual's total exposure to air pollution.

Some evidence suggests that indoor pollution may be related to childhood illness.[1,2] In addition, differences in respiratory symptoms and ventilatory function between black and white children,[3] and the intersubject variability in respiratory illness and lung function in any given community may be partially explained by differences in indoor pollutant exposures. We examined the relationship, if any, between personal pollutant load and respiratory disease.

Materials and Methods

From April through June 1973, 265 children (102 boys, 163 girls) aged 12 to 17 years were seen as part of a community respiratory disease survey in Ansonia, Connecticut.[4] From the 102 boys in the survey, 5 black and 5 white subjects with respiratory disease were randomly chosen, together with 5 black and 5 white normal control subjects matched for age within the racial group. All subjects were nonsmokers and had lived in the area for at least the preceding 5 years. Criteria for selection in the disease groups were: 1) cough on most days, 2) wheezing at least once a month, and/or 4) a history of asthma. The presence of respiratory disease was corroborated by pulmonary function tests. The personal air sampling equipment was contained in a ...

56 cm by 41 cm by 15 cm (22 in by 16 in by 6 in) suitcase weighing 10 kg (22 lb). This sampler could be carried by a subject wherever he went and positioned to take in air at breathing level. Based on a system developed by Burgess and associates,[5] the sampler was modified in this laboratory to sample continuously for 24 hours, without significant fluctuations in air flow rates, after having been connected to an AC power supply for the previous 16 hours. Three separate samples were drawn, for suspended respirable particulates, sulfur dioxide (SO_2), and nitrogen dioxide (NO_2).

Particulates were collected on a millipore filter (pore size, 0.8 μm) with the aid of an MSA cyclone sampler (respirable dust (particulates less than 7 μm in diameter). The filters, after being conditioned to standard temperature and humidity, were weighed to the nearest 10 μg before and after the sampling period. SO_2 and NO_2 were analyzed by accepted methods.

Subjects carried the sampler with them for a 24-hour period on a day when they attended school. The sampler can continuously and was taken to all activities including the walk to and from school, gym class, and meeting, sports, or any other after-school activities. At the end of the 24-hour sampling period, we recorded the daily activities, and details of the climatic conditions and the home environment, including the number of smokers in the home, the number of people and rooms in the home, the type of heating system used, the type of fuel used for cooking, the composition of the floor or floor covering, the presence or absence of open or closed windows, and the presence or absence of a fireplace and pets. Two subjects reported an atypical exposure or daily activity. In both of these situations the data were rejected and the sampling repeated.

In addition to the personal air sampling, outdoor sampling according to standard technique was conducted continuously as part of the community respiratory disease survey in Ansonia.[6] These outdoor measurements were taken

Table 1—Personal Air Pollution Measurements by Race and Control or Disease Status, and by Presence of One or More Smokers in the Home

	No. of Subjects	Particulates ($\mu g/m^3$)	SO_2 ($\mu g/m^3$)	NO_2 ($\mu g/m^3$)
Race				
Black				
Control	5	123 ± 33	5.7 ± 1.5	73 ± 18
Disease	5	96 ± 13	6.6 ± 2.1	58 ± 3.6
White				
Control	5	131 ± 28	4.9 ± 0.9	53 ± 12
Disease	5	108 ± 25	5.0 ± 1.2	59 ± 21
Smokers in home				
No	9	95 ± 13	5.7 ± 1.1	53 ± 9.3
Yes	11	132 ± 21	5.4 ± 0.2	68 ± 11

NOTE: Measurements given as mean ± SE.
*P<.05; significant difference in mean particulate concentration between the two domestic smoking groups, using the t-test with the Cox-Cochran correction for unequal variances.

within 2 miles of the homes and schools of the subjects under study. Subsequent to the personal monitoring, these subjects were studied with simultaneous indoor and outdoor particulate measurements. The personal air sampler was used in the home for indoor sampling, and a Hi-Vol sampler was used at a distance of from 4 to 6 meters from the home for outdoor sampling. These simultaneous comparisons were made over a 24-hour period.

The study was conducted from September through December 1973.

Results

Table 1 shows the mean personal air pollution measurements for all groups. The individual exposures varied widely, as reflected in the high standard error of the mean for most measurements. Compared to the Environmental Protection Agency air quality standards (EPAAQS), these mean results were high for particulates, very low for SO_2, and moderately low for NO_2 (EPAAQS annual geometric means are 75 $\mu g/m^3$, 80 $\mu g/m^3$, and 100 $\mu g/m^3$, for particulates, SO_2, and NO_2, respectively).

The mean particulate concentrations for subjects exposed to domestic cigarette or cigar smoke were significantly higher ($t = 2.61$; $P < .05$) than those for subjects not so exposed (Table 1). Even in the latter group, particulate exposure was high, exceeding the EPAAQS of 75 $\mu g/m^3$ for all but one subject, for whom particulates were 48 $\mu g/m^3$. Exposure to NO_2 also tended to be greater in children exposed to domestic smoking. There was no significant difference between the two groups with respect to mean SO_2 exposure or pulmonary function, measured as the ratio of forced expiratory volume in 1 second to the forced vital capacity ($FEV_{1.0}$/

FVC), and the ratio of the maximum expiratory flow at 50% of lung volume to the FVC (MEF50%/FVC).

Particulate exposure tended to be higher in subjects living in homes with higher ratio of persons to number of rooms, but the association was not significant. No correlation was observed between pollutant levels and the other home factors recorded.

A comparison of disease and control groups showed higher particulate exposure among control subjects. However, this difference was not statistically significant and was reduced when the presence of domestic smoking was taken into account. There were no significant differences in pollutant exposures between black and white children.

Table 2—Comparison of Personal and Outdoor Environmental Measurements

Pollutant	Concentration Levels (Mean ± SE)	
	Personal	Outdoor
Particulates	114.5 ± 9.9	58.4 ± 3.9 ‡
SO_2	5.5 ± 0.7	12.0 ± 2.8
NO_2	61.3 ± 7.2	100.1 ± 9.0 //

NOTE: Data given in $\mu g/m^3$.
*Data for all pollutants based on twenty measurements.
†Data for particulate concentration based on twenty-two measurements; data for SO_2 and NO_2 concentration based on twenty-one measurements.
‡P<.001. §P<.05. //P<.01; significant difference in mean pollutant concentration between the two groups, by Student's t-test and the t-test with the Cox-Cochran correction for unequal variances.

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Table 2 shows the average pollutant concentrations obtained with the personal sampler and those of the outdoor air measured in the same area during the 2-month study period. In-home measurements of particulate levels for three subjects living in homes with smokers were (in $\mu g/m^3$): subject 1, 112; subject 2, 57; subject 3, 141. Simultaneous measurements taken outside the home for the same subjects 1, 2, and 3 were (in $\mu g/m^3$) 26, 48, and 61, respectively. Subjects 1 and 3 reported no respiratory symptoms, while subject 2 reported cough on most days.

Comment

We found that personal exposures to particulates were considerably higher than outdoor concentrations; in all but one subject, they exceeded the present annual EPAAQS. On one occasion, particulate exposure exceeded the maximum 24-hour concentration allowed not more than once per year (260 $\mu g/m^3$). This is particularly interesting since the personal sampler is designed to measure only particulates less than 7 μm in diameter, while the outside and EPAAQS levels reflect particles in the range of 0.1-100 μm. On the average, personal SO_2 and NO_2 levels were well below outdoor levels and the EPAAQS. Previous investigations have reported similar findings for NO_2, but not for particulates. Yocom et al. also present data supporting the presence of indoor particulate and SO_2 sources.

The large variance among the individual exposures probably reflects true variation in personal air pollution loads. The subjects used in the study were cooperative, and the sampler was always locked to prevent interference. In general, the errors of measurement in the methods of pollutant analysis we used are smaller than the variations between subjects that we observed. However, variation in millipore filter weight with small changes in humidity may account for some of the variance noted in the particulate measurements. This problem can be overcome by using glass-fiber filters, which are less hygroscopic.

We could not find a relation between personal pollutant exposure and variation in climate. However, the study was conducted during a single season, and the indoor environment is probably protected from gross climatic influences.

[illegible text] Analysis of cigarette particulate emissions has shown that indoor smoking can lead to high particulate emissions. An individual's exposure will depend on ventilation of the home and on his distance from a smoker. It has been suggested that cigarette smoking may cause increased NO_2 levels in a confined space. NO_2 concentrations found in the homes of smokers tended to be higher than in the homes of nonsmokers. The ratio of persons to number of rooms in the home may also influence particulate exposure.

In general, pollutant exposure was similar for control and disease subjects. [illegible]

disease. We found no evidence to support a cause and effect relationship between pollutant exposure and respiratory disease.

Outdoor air measurements do not accurately reflect the air pollution load experienced by individuals who live in the area of sampling. Children probably spend more time outdoors than most adults; nevertheless, our analysis of reported daily activities showed that children are indoors from at least 60% to about 80% of an average school day. Therefore, indoor pollutant exposures, especially to cigarette smoke, are of particular interest. In this study, nineteen of the twenty children had a 24-hour particulate exposure higher than the annual mean of the primary air quality standard (75 $\mu g/m^3$), even though outdoor levels at this time were lower than the standard. Since a person's air pollutant load, especially for respirable particulate, appears to be determined primarily by indoor exposure, no significant improvement in respirable particulate load can be expected to result from reduction of outdoor particulate levels, even in urban areas.

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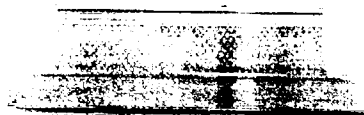
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Dyspnoea on exertion				Asthmatic attacks				Rhinitis				D+C+, D+C-, D-C+			
1–5 ×		0 ×		1–5 ×		0 ×		1–5 ×		0 ×		1–5 ×		0 ×	
V	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%
84	51.2	194	14.4	36	87.8	142	18.3	62	42.2	116	17.4	101	51.0	77	12.5
111	67.7	197	30.2	35	85.3	273	35.3	97	66.0	211	31.6	135	68.2	173	28.0
35	21.3	48	7.3	11	26.8	72	9.3	21	14.3	62	9.3	38	19.2	45	7.3
87	53.0	119	18.3	35	85.3	171	22.1	64	43.5	142	21.2	103	52.0	103	16.7
73	44.5	65	10.0	28	68.3	110	14.2	43	32.7	90	13.5	87	43.9	51	8.3
81	49.3	34	5.2	28	68.3	87	11.2	53	36.1	62	9.3	91	45.9	24	3.9
18	11.0	99	1.4	18	43.9	9	1.2	10	6.8	17	2.5	25	12.6	2	0.3
14	8.5	8	1.2	13	31.7	9	1.2	9	6.1	13	1.9	20	10.1	2	0.3
164		651		41		774		147		668		198		617	

Table 12. *Pulmonary function values according to symptom and age (population A + B)*

Age (years)	Cough >3 months a year			Cough >3 consecutive months a year			Cough 2 consecutive months a year			Cough 1 consecutive month a year		
	N	Mean $\frac{FEV_1}{FEV_1(E)}$ %	Mean FEV₁ %	N	Mean $\frac{FEV_1}{FEV_1(E)}$ %	Mean FEV₁ %	N	Mean $\frac{FEV_1}{FEV_1(E)}$ %	Mean FEV₁ %	N	Mean $\frac{FEV_1}{FEV_1(E)}$ %	Mean FEV₁ %
6/7	0			0			0			0		
7/8	2	84	79	0			0	96	81	4	93	81
8/9	27	93	78	13	98	79	8	96	81	18	93	80
9/10	25	93	79	12	96	80	11	95	80	25	94	77
10/11	20	97	80	10	97	78	2	84	76	12	98	78
11/12	17	94	80	8	96	79	0			0		
12/13	16	94	79	9	93	78	4	100	85	14	92	75
13/14	14	99	78	5	95	75	2	116	84	22	99	80
14/15	15	106	79	5	101	77	6	107	80	18	113	81
15/16	18	98	73	9	101	73	2	98	79	10	104	76

Age (years)	Dyspnoea on exertion			Asthmatic attacks			Rhinitis		
	N	Mean $\frac{FEV_1}{FEV_1(E)}$ %	Mean FEV₁ %	N	Mean $\frac{FEV_1}{FEV_1(E)}$ %	Mean FEV₁ %	N	Mean $\frac{FEV_1}{FEV_1(E)}$ %	Mean FEV₁ %
6/7	0			0			0		
7/8	4	94	83	0			6	96	78
8/9	53	96	79	5	90	74	51	95	79
9/10	60	93	79	6	93	78	45	95	79
10/11	36	93	78	6	82	72	32	96	79
11/12	18	92	76	12	88	74	16	93	80
12/13	62	93	78	8	91	72	23	93	77
13/14	49	98	78	7	94	75	26	95	79
14/15	56	100	78	7	84	67	19	96	77
15/16	35	99	76	4	89	64	29	103	77

Age (years)	D+C+ D−C+ᵃ D+C−			D−C− (c and/or w and/or n +)ᵃ			D−C− (c−w−n−)ᵃ		
	N	Mean $\frac{FEV_1}{FEV_1(E)}$ %	Mean FEV₁ %	N	Mean $\frac{FEV_1}{FEV_1(E)}$ %	Mean FEV₁ %	N	Mean $\frac{FEV_1}{FEV_1(E)}$ %	Mean FEV₁ %
6/7	0	94	83	0	97	79	0	96	81
7/8	4	94	83	14	97	79	56	96	81
8/9	60	96	79	111	99	81	335	99	82
9/10	63	93	79	95	95	78	358	99	81
10/11	47	94	78	93	97	79	366	97	80
11/12	27	93	77	51	98	82	283	96	81
12/13	66	93	78	59	93	79	306	95	81
13/14	50	98	77	68	98	80	271	100	81
14/15	59	100	78	55	105	80	285	104	81
15/16	43	101	76	49	106	80	287	105	80

ᵃ Criteria: see text p. 15.

ᵇ FEV₁(E) estimated FEV₁ of children from the same population without a present or past history of respiratory disease according to the formula's: *Boys:* ¹⁰log FEV₁(E) = −3.37740 + 2.63690 · ¹⁰log height (cm) in cl; *Girls:* ¹⁰log FEV₁(E) = −4.25738 + 3.03284 · ¹⁰log height (cm) in cl.

Table 13. *Pulmonary function values according to symptoms and numbers of years with symptoms (population A + B)*

Both birth cohorts are taken together

Number of years	Cough ≥3 months a year			Cough ≥3 consecutive months a year			Cough 2 consecutive months a year			Cough 1 month a year		
	N	Mean FEV₁ FEV₁(E)	Mean FEV₁ %	N	Mean FEV₁ FEV₁(E)	Mean FEV₁ %	N	Mean FEV₁ FEV₁(E)	Mean FEV₁ %	N	Mean FEV₁ FEV₁(E)	Mean FEV₁ VC %
0	756	99	81	831	99	81	866	99	80	786	99	80
1	95	97	80	56	97	78	41	96	79	108	98	80
2	36	93	77	18	92	76	3	95	77	12	95	80
3	15	92	77	0			1	93	70	3	94	79
4	3	89	76	1	99	78	0			1	92	81
5	2	90	74	1	110	75	0			0		

Number of years	Dyspnoea on exertion			Asthmatic attacks			Rhinitis		
	N	Mean FEV₁ FEV₁(E)	Mean FEV₁ %	N	Mean FEV₁ FEV₁(E)	Mean FEV₁ %	N	Mean FEV₁ FEV₁(E)	Mean FEV₁ %
0	709	99	81	852	99	81	732	99	81
1	86	96	79	41	96	78	85	97	79
2	47	98	80	8	90	72	44	96	78
3	29	98	79	2	90	66	24	97	82
4	28	94	76	3	81	67	13	93	76
5	8	89	73	1	80	70	9	90	73

Number of years	D+C = D–C +ᵃ D : C–			D–C– (C and/or N and/or W+)ᵃ			D–C– (C–N–W–)ᵃ		
	N	Mean FEV₁ FEV₁(E)	Mean FEV₁ %	N	Mean FEV₁ FEV₁(E)	Mean FEV₁ %	N	Mean FEV₁ FEV₁(E)	Mean FEV₁ %
0	671	100	81	489	99	81	86	95	78
1	103	95	79	210	99	80	86	96	79
2	56	97	79	104	97	79	89	96	79
3	34	97	80	55	98	79	110	99	81
4	31	96	77	40	95	80	204	100	81
5	13	89	73	9	98	80	332	100	81

ᵃ Criteria: see text p. 15. For statistical evaluation see text p. 17.
ᵇ FEV₁(E) - estimated FEV₁ of children from the same population without a positive present and past history of respiratory symptoms, according to the formula's: *Boys:* ¹⁰log FEV₁(E) = –3.37740 + 2.63690 · ¹⁰log height (cm) in cl; *Girls:* ¹⁰log FEV₁(E) = –4.25738 + 3.03284 · ¹⁰log height (cm) in cl.

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Table 14. *Number and percentage of children according to median value of histamine threshold, symptoms and number of years with symptoms (population A + B)*

Only children with at least 3 histamine threshold values have been listed. In parenthesis: in % of total number (N).

Number of years	Cough >3 months a year				Cough >3 consecutive months a year				Cough 2 consecutive months a year			
	N	<8	16	>32	N	<8	16	>32	N	<8	16	>3
0	711	14 (2.0)	69 (9.7)	628 (88.3)	785	19 (2.4)	77 (9.8)	689 (87.8)	814	24 (2.9)	84 (10.3)	706 (86.7)
1	93	6 (6.4)	10 (10.7)	77 (82.8)	55	3 (5.4)	10 (18.2)	42 (76.3)	40	1 (2.5)	4 (10.0)	35 (87.5)
2	36	4 (11.1)	7 (19.4)	25 (69.4)	16	3 (18.8)	1 (6.2)	12 (75.0)	3	0	0	3
3	13	1	0	12	0	0	0	0	1	0	0	1
4	3	0	2	1	1	0	0	1	0	0	0	0
5	2	0	0	2	1	0	0	1				

Number of years	Cough consec. 1 month a year				Dyspnoea on exertion				Asthmatic attacks			
	N	<8	16	>32	N	<8	16	>32	N	<8	16	>32
0	735	22 (3.0)	67 (9.1)	646 (87.9)	666	8 (1.2)	55 (8.2)	603 (90.5)	806	15 (1.9)	74 (9.2)	717 (88.9)
1	108	3 (2.8)	18 (16.7)	87 (80.5)	85	6 (7.0)	7 (8.2)	72 (84.7)	40	5 (12.5)	11 (27.5)	24 (60.0)
2	11	0	1	10	44	3 (6.8)	13 (29.5)	28 (63.6)	8	3	2	3
3	3	0	2	1	29	2 (6.9)	8 (27.6)	19 (65.5)	1	0	1	0
4	1	0	0	1	27	4 (14.8)	5 (18.5)	18 (66.7)	2	1	0	9
5					7	2	0	5	1	1	0	0

Number of years	Rinitis				D+C+ D–C+* D+C–			
	N	<8	16	>32	N	<8	16	>32
0	686	13 (1.9)	60 (8.7)	613 (89.3)	628	8 (1.3)	46 (8.7)	574 (89.3)
1	82	5 (6.1)	9 (11.0)	68 (82.9)	103	5 (4.8)	13 (12.6)	85 (82.5)
2	45	3 (6.7)	9 (20.0)	33 (73.3)	52	2 (3.8)	15 (28.8)	35 (67.3)
3	23	1 (4.3)	5 (21.7)	17 (73.9)	34	3 (8.8)	6 (17.6)	25 (73.5)
4	13	1	2	10	29	2 (6.9)	8 (27.6)	19 (65.5)
5	9	2	3	4	12	5	0	7

* Criteria: see text p. 15. For statistical analysis see text page 19.

Table 15a. Number of children according to birth cohort and skin test reactions in 1968/69 and 1973 (population A + B)

In parenthesis: % of total number

	Birth cohort 1/10/60–30/9/61				Birth cohort 1/10/55–30/9/56			
	1968 1969	1973		Total	1968 1969	1973		Total
		Negative	Positive			Negative	Positive	
House dust								
Negative		182	30	212	Neg.	93	28	121
Positive		5	24	29 (12)	Pos.	2	28	30 (20)
Total		187	54 (22)	241	Total	95	56 (37)	151
Grass pollen								
Negative		219	16	235	Neg.	125	19	144
Positive		2	4	6 (2)	Pos.	1	6	7 (5)
Total		221	20 (8)	241	Total	126	25 (16)	151
Animal danders								
Negative		204	27	231	Neg.	115	17	132
Positive		3	7	10 (4)	Pos.	1	18	19 (12)
Total		207	34 (14)	241	Total	116	35 (23)	151

Table 15b. *Number of children according to number of years with symptoms and skin test reaction in 1968/69 and 1973 (population A + B)*
In parenthesis: in % of total. For statistical analysis; see text p. 22.

Skin tests[a]	68/69	73	Cough ≥ 3 months a year Number of years		Cough ≥ 3 consec. months a year Number of years		Cough 2 consec. months a year Number of years	
			0	≥ 1	0	≥ 1	0	≥ 1
House dust	−	+	48 (83)	10	52 (90)	6	56 (96)	2
	+	+	40 (78)	11	44 (86)	7	49 (96)	2
Grasspollen	−	+	26 (76)	8	28 (82)	6	33 (97)	1
	+	+	6 (60)	4	8 (80)	2	9 (90)	1
Animal danders	−	+	34 (72)	9	38 (88)	5	42 (98)	1
	+	+	17 (68)	8	18 (72)	7	24 (96)	1
All skin tests	−	−	219 (83)	46	242 (91)	23	250 (94)	15

[a] Means: concentration of house dust 0.5 mg/ml or less; concentration of grass-pollen 1 000 NE or less; concentration of animal danders 0.25 mg/ml or less.

Table 16. *Chest X-rays according to symptom groups (population A + B)*

Symptom-groups[a]	Line shadows				Mottled shadowing				
	Normal	In-creased	Un-known	Total	Not present	Present but not marked	Marked	Un-known	Total
D + C +	17	1	0	18	18	0	0	0	18
D + C −	93	0	0	93	92	0	1	0	93
D − C +	28	2	0	30	28	0	0	0	28
D − C −	1 022	4	6	1 032	1 020	5	0	6	1 031
Unknown	6	0	0	6	6	0	0	0	6
Total	1 166	7	6	1 179	1 164	5	1	6	1 176

[a] Criteria: see text p. 15.

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Cough 1 consecutive month a year Number of years		Dyspnoea on exertion Number of years		Asthmatic attacks Number of years		Rhinitis Number of years		D+C+ D-C+ D+C- Number of years		Total number
0	>1	0	>1	0	>1	0	>1	0	>1	
52 (90)	6	47 (81)	11	56 (96)	2	49 (84)	9	45 (77)	13	58
39 (76)	12	33 (65)	18	43 (84)	8	36 (71)	15	30 (59)	21	51
29 (85)	5	23 (68)	11	29 (85)	5	24 (71)	10	20 (59)	14	34
8 (80)	2	7 (70)	3	9 (90)	1	6 (60)	4	6 (60)	4	10
37 (86)	6	35 (81)	8	41 (95)	2	35 (81)	8	30 (70)	13	43
17 (68)	8	9 (36)	16	17 (68)	8	12 (48)	13	9 (36)	16	25
235 (88)	30	223 (84)	42	256 (97)	9	220 (83)	45	210 (79)	55	265

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Table 17a. *Correlation of symptoms in children and parents' smoking habits, 1972 (population A + B)*

In parenthesis: % of total

	D/C pos. groups[a]	D/C neg. groups[a]	Total
Both parents non smokers	20 (9)	211 (91)	231 (100)
One or both parents smokers	39 (9)	377 (91)	416 (100)
Total	59 (9)	588 (91)	647 (100)

[a] Criteria: see text p. 15.

Table 17b. *Correlation of symptoms in children and parents' smoking habits, 1972 (population A + B)*

In parenthesis: % of total

Average number of cigarettes per day, smoked by father or mother	D/C pos. groups[a]	D/C neg. groups[a]	Total
0	20 (9)	211 (91)	231 (100)
1–4	6 (12)	43 (88)	49 (100)
5–14	13 (8)	159 (92)	172 (100)
⩾15	20 (10)	175 (90)	195 (100)
Total	59 (9)	588 (91)	647 (100)

[a] Criteria: see text p. 15.

Table 18a. *Correlation of symptoms in parents and children 1972 (population A + B)*

Symptoms of parents	Symptoms of children			
	D+C+[d] %	D-C- c-w-n-[d] %	Total[e] N	Total[e] %
Father and/or mother + +[a]	68	33	121	100
Father and/or mother +[b]	57	43	169	100
Both parents negative[c]	47	53	328	100
Total[e]	54	46	618	100
P value of trend (χ^2)	<0.001			

[a] Cough on most days for as much as 3 consecutive months a year and/or Phlegm on most days for as much as 3 consecutive months a year and/or Breathlessness when walking at an ordinary pace on level ground and/or Asthmatic attacks.
[b] Cough usually first thing in the morning and/or Cough usually during the day or at night and/or Phlegm usually first thing in the morning and/or Phlegm usually during the day or at night and/or Breathlessness when hurrying on level ground.
[c] None of the above symptoms.
[d] Criteria see text p. 15.
[e] Only parents who answered all questions were taken into account.

Table 19b. *Correlation of parents' smoking habits and symptoms in parents and children, 1972 (population A + B)*

In parenthesis: % of total

Symptoms of parents	Both parents non smokers			One parent a smoker			Both parents smokers		
	Children D/C pos. groups[d] >1 year(s)	Children D/C pos. groups[d] 0 years	Total	Children D/C pos. groups[d] >1 year(s)	Children D/C pos. groups[d] 0 years	Total	Children D/C pos. groups[d] >1 year(s)	Children D/C pos. groups[d] 0 years	Total
Father and/or mother[a]	16 (70)	7 (30)	23 (100)	36 (62)	22 (38)	58 (100)	30 (75)	10 (25)	40 (100)
Father and/or mother[b]	17 (60)	11 (40)	28 (100)	36 (53)	32 (47)	68 (100)	43 (59)	30 (41)	73 (100)
Both parents negative[c]	48 (53)	43 (47)	91 (100)	60 (43)	79 (57)	139 (100)	46 (47)	52 (53)	98 (100)
Total	81 (57)	61 (43)	142 (100)	132 (50)	133 (50)	265 (100)	119 (56)	92 (44)	211 (100)
P value of trend (χ^2)	0.315			0.045			0.009		

[a] Cough on most days for as much as 3 consecutive months a year and/or
Phlegm on most days for as much as 3 consecutive months a year and/or
Breathlessness when walking at an ordinary pace on level ground and/or Asthmatic attacks.
[b] Cough usually first thing in the morning and/or Cough usually during the day or at night and/or
Phlegm usually first thing in the morning and/or Phlegm usually during the day or at night and/or
Breathlessness when hurrying on level ground.
[c] None of the above symptoms. [d] Criteria: see text p. 15.

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Table 20. *Prevalence of symptoms in children present in 1968 and 1972 and in children who dropped out*

	Cough >3 months per year		Cough >3 consec. months per year		Dyspnoea on exertion		Asthmatic attacks	
	N	%	N	%	N	%	N	%
1968, present	91	7.3	44	3.5	45	3.6	41	3.3
1969–1971, drop outs	22	5.1	12	2.8	10	2.3	13	3.0
1972, present	69	8.4	32	3.9	35	4.3	28	3.4

* Criteria see text p. 15.

Table 21. *Comparison of prevalence of symptom-positive groups with different criteria for cough, according to age (population A)*

D+ Affirmative answer to one or more of questions: 15, 24 (1968); 15, 18, 27, 29 (1969).
C+* Affirmative answer to one or more of questions: 4, 5 (1968); 6, 9 (1969).
C+** Affirmative answer to one or more of questions: 3, 4, 5 (1968); 5, 6, 7, 9, 10 (1969).

Age (years)	D+C+* D+C- D C+ %	D+C+** D+C+ D-C+ %
6/7	11.2	15.6
7/8	10.5	13.1
8/9	9.8	11.7
9/10	11.2	13.3
10/11	8.6	9.8
11/12	6.9	8.2
12/13	13.9	14.6
13/14	11.6	12.3
14/15	12.6	14.1
15/16	9.8	11.0

Table 22. *Comparison of prevalence of symptom-positive groups with different criteria for cough, according to number of years with symptoms (population A)*

D+ Affirmative answer to one or more of questions: 15, 24 (1968); 15, 18, 27, 29 (1969).
C+* Affirmative answer to one or more of questions: 4, 5 (1968); 6, 9 (1969).
C+** Affirmative answer to one or more of questions: 3, 4, 5 (1968); 5, 6, 7, 9, 10 (1969).

Numbers of years with symptoms	Birth cohort 1/10/60–30/9/61		Birth cohort 1/10/55–30/9/56	
	D+C+* D+C- D-C+ %	D+C+** D+C- D-C+ %	D+C+* D+C- D-C+ %	D+C+** D-C- D-C+ %
0	75.0	69.6	76.1	72.7
1	12.4	14.0	9.5	11.6
2	5.1	6.8	5.6	6.4
3	3.0	4.7	2.8	3.1
4	2.6	2.6	4.1	4.1
5	1.9	2.3	1.8	2.1

Rhinitis		D+C+ D+C+* D+C-		D-C-*		Total	
N	%	N	%	N	%	N	%
97	7.7	101	8.1	1 151	91.9	1 252	100
27	6.2	26	6.0	409	94.0	435	100
70	8.6	75	9.2	742	90.8	817	100

Table 23. *Comparison of prevalence of symptom-positive groups,[a] wheezing included (population A)*

Age (years)	D+C+* D+C- D-C+ W- %	D+C+* D+C- D-C+ W+ %	Age (years)	D+C+* D+C- D-C+ W- %	D+C+* D+C- D-C+ W+ %
6/7	11.1	16.8	11/12	6.9	9.5
7/8	10.3	16.1	12/13	14.1	16.2
8/9	9.8	15.6	13/14	11.2	15.1
9/10	11.3	16.3	14/15	12.8	15.1
10/11	8.9	14.7	15/16	9.3	16.5

[a] D-C+: Criteria see text p. 15. W+: Affirmative answer to one or more of questions 19 (1968); 23, 25 (1969).

Table 24. *Smoking habits per school level, birth cohort 55/56 (population A+B)*

V.W.O. praeuniversity education, HAVO higher general continued education, MAVO intermediate general continued education, LTS elementary technical school, Nijverheidsschool elementary domestic science school.

School or work	Smokers, % 1971	Smokers, % 1972	Number of cigarettes per day (average) 1971	Number of cigarettes per day (average) 1972	Age at which regular smoking started (average)
V.W.O.	36	20	3	10	13
HAVO	58	50	3	6	14
MAVO	50	55	3	5	13
Nijverheids-school	43	60	3	6	13
LTS	52	64	4	7	13
Unskilled	83	80	7	9	13
Total	51	57	4	7	13

Table 25. *Correlation of number of years with major respiratory symptoms and number of years with minor respiratory symptoms[a] (population A)* In parenthesis: %

Number of years with major symptoms[a]	Number of years positive with minor symptoms[a] 0	1	2	3	4	5	Total N %
0	354 (63)	113 (20)	50 (9)	23 (4)	14 (3)	8 (1)	562 (100)
1	51 (50)	23 (22)	10 (10)	10 (10)	9 (9)		103 (100)
2	17 (33)	17 (33)	10 (20)	7 (14)			51 (100)
3	14 (47)	11 (37)	5 (27)				30 (100)
4	14 (54)	12 (46)					26 (100)
5	18						18 (100)
Total	468	176	75	40	23	8	790 (100)

[a] See text p. 15.

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Rantakallio, P. "Relationship of Maternal Smoking to Morbidity and
Mortality of the Child Up to the Age of Five" Acta Paediatr Scand
67(5): 621-631, 1978.

ABSTRACT: The effect of maternal smoking during pregnancy
on the morbidity and mortality of the child up to the age of five
was studied in 12068 births. The children of the smokers were
compared with those of controls of similar age, parity, marital
status and place of residence. Perinatal mortality was no higher
among the smokers, but postneonatal mortality from 28 days to 5
years was almost significantly ($p < 0.05$) higher. The children of
the smokers were highly significantly ($p < 0.001$) more often
hospitalized in pediatric departments, the difference being clearest
below the age of one. The average duration of hospital admissions
was longer among the children of the smokers, and similarly the
numbers of visits to the doctor and hospital admissions to any
hospital under the age of one were more frequent among the children
of the smokers. Respiratory diseases caused highly significantly
more hospitalizations among these children.

RELATIONSHIP OF MATERNAL SMOKING TO MORBIDITY AND MORTALITY OF THE CHILD UP TO THE AGE OF FIVE

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ABSTRACT. Rantakallio, P. (Department of Paediatrics and Department of Public Health, University of Oulu, Oulu, Finland). Relationship of maternal smoking to morbidity and mortality of the child up to the age of five. Acta Paediatr Scand, 67: 621, 1978.—The effect of maternal smoking during pregnancy on the morbidity and mortality of the child up to the age of five was studied in 12 068 births. The children of the smokers were compared with those of controls of similar age, parity, marital status and place of residence. Perinatal mortality was no higher among the smokers, but postneonatal mortality from 28 days to 5 years was almost significantly $(p < 0.05)$ high .... respiratory diseases caused highly significantly more hospitalizations .... children.

KEY WORDS: Maternal smoking, perinatal mortality, childhood mortality, hospital admission, out-patient visits, respiratory diseases

The fact that maternal smoking during pregnancy lowers the birth weight of the offspring is well documented. Studies on the relationship between maternal smoking and perinatal mortality are also numerous, even though the findings still contain some contradictory points (1–4, 8–12, 15, 17, 19–21, 25, 26, 31, 32, 37–40). Studies on the correlation between maternal smoking and morbidity and mortality during later childhood are relatively rare, however. Comstock & Lundin (8) reports that the childhood mortality rate up to the age of 11 was higher among children whose mothers smoked, and impaired health in the children of smokers has been investigated in several studies (5, 7, 13, 18).

The present study investigates the effect of maternal smoking on morbidity and mortality up to age of five in a series from Northern Finland in which maternal smoking habits were recorded during pregnancy.

MATERIALS AND METHOD

The series consists of 12 068 pregnant mothers from the two northernmost provinces of Finland, Oulu and Lapland. The investigation was started at the sixth or seventh month of pregnancy in the antenatal clinics and covered 96% of all deliveries in 1966 (26). Twin births numbered 163 and single births 11 905. The many biological and socio-economic characteristics of the mother and family which were examined included the mother's smoking habits. Each mother was asked whether she had been a regular smoker before pregnancy, and if so, how much she had smoked, whether she had changed her habits during pregnancy, and if so, how.

The mothers were divided into three categories in the following way:

(a) *non-smokers*, those who never smoked or who had stopped smoking during the first two months of pregnancy,

(b) *light smokers*, who smoked less than 10 cigarettes per day at the end of the second month of pregnancy, and

(c) *heavy smokers*, who smoked 10 or more cigarettes per day at the end of the second month of pregnancy.

In 554 mothers (4.6%) smoking data was lacking or incomplete, or in a few cases inclassifiable, e.g. when the mother did not smoke at the beginning of pregnancy but started later. The non-smokers amounted to 9 695 mothers 80.3% of the total, and comprised 9 176 who had never

Table 1. *Perinatal mortality among the smokers and their controls*
Series is divided into social groups according to father's occupation*

	Smokers				Controls			
Social group	Still-births	Neonatal deaths, first 28 days	All births	Perinatal mortality per 1000	Still-births	Neonatal deaths, first 28 days	All births	Perinatal mortality per 1000
I+II	4	5	320	28.1	4	5	402	22.4
III+IV	16	14	1 197	25.1	10	11	1 074	19.6
Farmers	1	3	157	25.5	4	4	205	39.0
Not known*	2	3	170	29.4	3	3	163	36.8
Total	23	25	1 844	26.0	21	23	1 844	23.9

* Based on the social standing of the occupation in question (36).
* Mostly mother unmarried.

smoked and 519 who had stopped smoking during the first two months of pregnancy. The mothers who smoked totalled 1 819; 1 515 or 12.6% of the total number smoked less than 10 cigarettes per day, while 304 (2.5%) smoked at least 10 cigarettes per day.

The mean number of cigarettes smoked per day by the light smokers was 5.2 at the beginning of pregnancy and 3.9 in the middle of pregnancy. The corresponding figures for the heavy smokers were 15.3 and 12.2 respectively.

A control was chosen for each mother who smoked from among the non-smokers, so that the number of children born was the same, the marital status was the same, the age was the same within a range of ±2 years and the parity was the same if it was 1, and otherwise of the same order, II or III, IV or V, and VI or over. The place of residence was checked for similarity on three scores: situated in the same province, having the same level of public services, taxable incomes of families and other development scores (24), all the 81 communes of the area being divided into four classes, and being similar in population density (town–village–remote village). By this manoeuvre 1 750 mothers out of the total of 1 819 were assigned controls, and 69 remained for whom it was impossible to find one. For these the limits of dissimilarity were widened in one or two of the characteristics with exception of the number of children born, marital status and parity 1 and VI+, in which the limits were kept as indicated.

All hospitalizations of the study children in the pediatric departments of the four central hospitals in the area were recorded by the members of the study group in 1972. By the time the child concerned had reached the age of 4, 7.6% of the families of the smokers and 7.0% of those of controls had moved out of the study area. No inquiries were made concerning hospitalizations outside study area. The analysis of the diagnoses given during hospitalization employs largely the main categories of diseases, and these are grouped on the basis of the manual for the statistical classification of diseases and injuries (6) in official use in Finland since 1969, which was in turn compiled with reference to the recommendations of WHO. The classification is identical with that in use in Sweden,

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but differs in certain minor respects from the International Classification of Disease, 1965 revision of WHO (14).

A questionnaire concerning the growth, development and health of the children at the ages of 6 and 12 months was sent to the children welfare centres in the study area in 1967. This was returned by 85.3% of the smokers and 85.6% of the controls. In this connection all visits to the doctor and hospitalizations in departments other than pediatric departments in central hospitals and all admissions to local hospitals supervised by a general practitioner were recorded.

The data concerning deaths up to the age of 5 years were collected from the Population Registration Centre and the causes of death from the Central Statistical Office. Since the great majority of deaths occurred before 1969, the earlier edition of the classification of diseases (22) was used in grouping the causes of death. From the point of this series, the greatest difference between the two editions lies in the "causes of perinatal morbidity and mortality", the former revision classifying most of the infectious diseases during the first 28 days into this group. Thus under this system practically all causes of death others than accidents and congenital malformations during the first 28 days were classified into this category.

Stillbirths were recorded at the postnatal clinics in connection with the other data (26), and as of 1966, all dead foetuses with a birth weight of 600 g or over were recorded as stillbirths in Finland.

The follow-up studies concerned the whole study group, not only the smokers and their controls. In testing significance the Student's *t*-test was used.

RESULTS

The smokers had 1 821 live-birth children and the controls 1 823. There was no statistically significant difference in the number of boys and girls born to the different smoking groups, nor was there any difference in the number of twin pregnancies.

Table 2. *Postneonatal mortality from 28 days to 5 years among the smokers and their controls*
Series is divided into social groups according to father's occupation*

Social group	Smokers			Controls		
	Deaths (N)	Alive after neonatal period (N)	Per 1000	Deaths (N)	Alive after neonatal period (N)	Per 1000
I+II	2	311	6.4	2	393	5.1
III+IV	13	1 167	11.1	4	1 053	3.8
Farmers	2	153	13.1	0	197	0.0
Not known*	3	165	18.2	1	157	6.4
Total	20	1 796	11.1	7	1 800	3.9

* Based on the social standing of the occupation in question (36).
* Mostly mother unmarried.

Perinatal mortality in smokers and controls by social groups is presented in Table 1. The difference between groups was not statistically significant either for the total groups or subgroups. The effect of the slightly different distribution into social groups among the smokers and controls was checked by repeating the calculation using the mortality rate of the controls and the total number of cases among the smokers for each social group. The perinatal mortality was thus 23.4 per thousand instead of the true figure 23.9 per thousand in the controls, the difference being without significance. The mortality rate was higher among the heavy smokers than in the other groups, 32.6 for the heavy smokers and 25.7 per thousand for the light smokers, but the difference was without statistical significance.

Table 2 depicts the *postneonatal mortality* in ~~these groups. The difference between social groups of smokers and controls was statistically almost significant ($p < 0.05$). The difference was noticeable in each social group except~~ ~~deaths highest.~~ When the postneonatal mortality was calculated for the controls for the case in which the distribution into social groups would be the same as among the smokers the result was not affected, being 3.9 per thousand. The figures for heavy and light smokers were about the same, 13.0 and 11.1 per thousand respectively.

Visits to the doctor and *hospital admissions* to any hospital in the area were recorded up to age of one year for 1 554 children of smokers and 1 560 children of controls. As may be seen from the results presented in Table 3, the chil-

Table 3. *Visits to the doctor and hospital admissions at the age of under one year, by smoking groups*
Visits to all hospitals in the study area are included

	Number of live births	Visits to the doctor			Hospitalizations		
		Children (N)	Visits (N)	Visits, mean for group	Children (N)	Visits (N)	Visits, mean for group
Light smokers	1 302	712	986	0.76	223	292	0.22
Controls	1 300	672⁻	927*	0.71⁻	190⁻	253⁻	0.19⁻
Heavy smokers	252	160	210	0.83	70	98	0.39
Controls	258	120***	157***	0.61**	33***	38***	0.15***
All smokers	1 554	872	1 196	0.77	293	390	0.25
Controls	1 558	792**	1 084***	0.69*	223***	291***	0.19**

⁻$p > 0.05$, *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$.

Table 4. *Hospital admissions by smoking groups*

Admissions to the pediatric departments of the four central hospitals in the study area

	Alive at age		Age under one			Age one to five		
	0 year (N)	1 year (N)	Children (N)	Visits (N)	Mean for group	Children (N)	Visits (N)	Mean for group
Light smokers	1 518	1 486	207	263	0.17	209	320	0.22
Controls	1 520	1 499	170*	209**	0.14*	154**	231***	0.15*
Heavy smokers	303	295	63	90	0.30	40	73	0.25
Controls	303	299	22***	25***	0.08***	42⁻	50*	0.17⁻
All smokers	1 821	1 781	270	353	0.19	249	393	0.22
Controls	1 823	1 798	192***	234***	0.13***	196**	281***	0.16**

$^-p>0.05$, $^*p<0.05$, $^{**}p<0.01$, $^{***}p<0.001$.

ren of the smokers visited the doctor more often and were more often admitted to the hospital than those of the controls, the difference in the number of children, visits and means for the groups having a certain degree of statistical significance. It is also clear that the differences are chiefly attributable to the effect of the heavy smokers.

the group of heavy smokers in the case of children of under one year, but this was no longer true for the age from one to five years. The difference between the smokers and the controls in the percentage of children hospitalized during their first day was almost significant (p<0.10) the figures being 7.6% in former and 5.9% in the latter group.

Hospital admission to the pediatric departments of the four central hospitals in the area were recorded for all children born to the smokers and controls (1 821 and 1 823). The results are presented in Table 4 separately for age under one year and for age from one to five. The children of the smokers had significantly more hospital admissions than those of the controls. The difference was more due to

Table 5 presents the number of children hospitalized per thousand live births among the smokers and controls by social groups. The children of each social group were more often hospitalized in the latter of smokers during pregnancy than in the others, with the exception of the group of more well-to-do farmers. In the case that the total number of cases among the controls had distributed into social

Table 5. *The children of the smokers and their controls admitted to pediatric departments during the first 5 years of life*

Series is divided into social groups according to father's occupation*

	Smokers (N 1821)		Controls (N 1823)	
Social group	Hospitalized children	Per thousand live births	Hospitalized children	Per thousand live births
I	14	202.9	20	170.9
II	58	234.8	44	156.6
III	185	265.0	137	213.4
IV	114	236.0	85	201.4
Farmers I*	5	102.0	12	131.9
Farmers II	29	271.0	23	209.1
Not known*	43	256.0	22	137.5
Total	448	246.0	343	188.2

* Based on the social standing of the occupation in question (36).
* Land under cultivation 8 hectares or over.
* Mostly mother unmarried.

Table 6. *Incidence of diseases during the first 5 years among the children of the smokers and the controls*

Incidence is based on all diagnoses given during hospital admissions in pediatric departments

Diagnosis	Smokers (N 1821)		Controls (N 1823)	
	N	Per thousand live births	N	Per thousand live births
Infective and parasitic dis.	118	64.8	103	56.5
Neoplasms	3	1.6	5	2.7
Endocrine, nutritional, and metabolic dis.	23	12.6	21	11.5
Dis. of the blood and bloodforming organs	85	46.7	48	26.3**
Mental disorders	5	2.7	11	6.0
Dis. of the nervous system and sense organs	90	49.4	52	28.5**
Dis. of the circulatory system	3	1.6	6	3.3
Dis. of the respiratory system —	311	170.8	179	98.2***
Dis. of the digestive system	39	21.4	34	18.7
Dis. of the genito-urinary system	53	29.1	33	18.1*
Dis. of the skin and subcutaneous tissue	41	22.5	15	8.2***
Dis. of the musculoskeletal system and connective tissue	11	6.0	4	2.2
Congenital anomalies	44	24.2	51	28.0
Causes of perinatal morbidity and mortality	176	96.6	128	70.2**
Symptoms and ill-defined conditions	67	36.8	54	29.6
Accidents, poisonings and violence	39	21.4	25	13.7
Examination and investigation	14	7.7	12	6.6
Total	1 122	616.1	781	428.4

$*p<0.05$, $**p<0.01$, $***p<0.001$.

groups as those of the smokers, 191.5 instead of 188.2 children per thousand had been hospitalized among the controls, the difference being without significance.

The mean duration of hospitalization was 14.0 days for the children of the smokers and 13.4 days for those of the controls, the difference being statistically highly significant. The mean duration of hospitalizations among the heavy smokers was 14.9 days, among the light smokers 13.7 days.

Table 6 presents the *frequency of all disease groups* diagnosed in children's departments *per thousand live births* among the children of smokers and of their controls. If the child had been in hospital more than once for the same disease it was counted only once. Respiratory and skin diseases were more frequent among the smokers than among the controls, the difference being statistically highly significant (p<0.001) and the children of smokers also had blood and nervous diseases and disease of the newborn period more often, the difference being statistically significant (p<0.01). Among

the respiratory diseases the ratio of the incidence among the smokers to that of the controls was 2.2 in pneumonia and bronchitis, and 1.5 in others such as acute nasopharyngitis, sinusitis etc. In addition, two cases of pulmonary atelectasis and one of empyema were recorded among the smokers but none among the controls.

Among the skin diseases the ratio of the incidence among the smokers to that among the controls was 2.7 in eczema and urticaria, and 2.0 in infectious disease of the skin and subcutaneous tissue and other diseases of this category.

Under the age of one year the difference in the diseases was in general greater between the heavy smokers and their controls than between the light smokers and their controls, but this was no longer true for the age from one to five.

When the *main causes* of hospitalization in pediatric departments per thousand live births was calculated for both groups a statistically highly significant difference (p<0.001) was

Table 7. *Causes of death at age under five years among the children of the smokers and their controls*

Diagnosis	Smokers (N 1821)		Controls (N 1823)	
	N	Per thousand live births	N	Per thousand live births
Infective and parasitic dis.	4	2.20	0	0.00
Neoplasms	2	1.10	1	0.55
Mental disorders	0	0.00	1*	0.55
Dis. of the nervous system and sense organs	4	2.20	1	0.55
Dis. of the respiratory system	5	2.75	1	0.55
Dis. of the digestive system	0	0.00	1	0.55
Dis. of the genito-urinary system	0	0.00	0	0.00
Congenital anomalies	4	2.20	7	3.84
Causes of perinatal morbidity and mortality	23	12.63	16	8.78
Accidents, poisonings, and violence	3	1.65	2	1.10
Total	45	24.71	30	16.47

* Down's syndrome.

found only in the case of respiratory diseases and an almost significant difference ($p<0.05$) in the case of skin diseases. The more frequent hospitalization of the children of smokers because of respiratory diseases was clearest below the age of one, but also existed at the age of one to five, the difference between the smokers and controls at that age being almost significant ($p<0.05$). Again the children of the heavy smokers were more affected than those of the light smokers under the age of one, but not at the age of one to five.

Since the higher frequency of other disease groups than respiratory diseases diagnosed among the children of smokers might be the result of more frequent hospitalization in the case of respiratory diseases, the differences in the frequencies of skin, blood, and nervous diseases and sense organs and diseases of the newborn period between the smokers and their controls were also calculated excluding those hospitalizations in which the main diagnosis was respiratory disease. In this case the difference in skin diseases was statistically significant ($p<0.01$) those in diseases of the newborn period and nervous diseases almost significant ($p<0.05$) and that in blood diseases without significance.

The hospital visits were studied *by seasons of the year* taking the months from November

to March as winter, from May to September as summer and the rest combined as the spring and autumn period. The difference between the smokers and the controls in the mean number of hospitalizations per child was significant in summer, significant in winter and almost significant in spring and autumn period. No clear trend was found for hospital admissions due to respiratory diseases to be any more accentuated among the children of smokers during the winter, even though the absolute figures for hospital admissions because of respiratory diseases were certainly greater during the winter both for the smokers and the controls.

In the diagnoses given during admission to any hospital in the area in the case of children under one year of age a highly significant difference ($p<0.001$) was found between the children of the smokers and those of the controls in respiratory diseases, the frequencies being 88.1 and 43.5 per thousand respectively. In blood diseases the differences was almost significant ($p<0.05$).

In causes of visits to the doctor under one year of age the children of the smokers had a statistically almost significant ($p<0.05$) higher frequency for respiratory diseases, blood diseases, diseases of genitourinary system and the group of endocrine, nutritional

and metabolic diseases. The frequency of respiratory diseases was 435.3 per thousand among the children of the smokers and 390.2 per thousand among the controls.

45 children of smokers and 30 children of controls died before the age of 5 years. The causes of death, calculated per thousand live births, are seen in Table 7. 38 children of the smokers and 29 children of the controls were in hospital at the time of death. The recorded cause of death was based on autopsy in 59 cases. Among the 8 cases who were not in hospital at the time of death, 4 were accidental deaths and 2 died of pneumonia, 1 of meningococcal septicaemia and 1 of cerebral palsy. The disease groups which were commonest among the children of smokers [illegible] high frequency among [illegible] of [illegible] cases [illegible] among [controls?] but the differences were not statistically significant.

DISCUSSION

The number of smokers in this series is considerably lower than in most other series reported. Goldstein (12) has tabulated the figures for the six largest series commonly referred to in connection with maternal smoking and its effect on the foetus and the child, having as the lowest percentage of smokers at the beginning of pregnancy the 21 % of this series (26), while the figures in the other series vary from 32 to 54 %. During the two first months of pregnancy the number of smokers in this series had dropped to 15.1 %.

The average *number of cigarettes smoked* in this series was probably also lower than in the other series, even though it is not easy to make comparisons with other studies because of the different criteria used for the classification into light and heavy smokers. For example, the Ontario Perinatal Mortality study (20) used the maximum number smoked per day any time during pregnancy, the light smokers being those who smoked less than one packet and those who smoked less than one packet and the heavy smokers those who smoked more than one packet. Thus the group classified in this series as heavy smokers may show more similarity with the light smokers than the heavy smokers in the Ontario study.

According to Butler & Goldstein (4) *abandonment of smoking* by the fourth month *of pregnancy* gives a mortality risk and expected birth weight comparable to those for mothers who are not smokers. The findings of Donovan (10) are, however, not in full agreement with this. In an earlier analysis of this series (26) it was shown that perinatal mortality was not significantly higher among smokers than among non-smokers when the group of smokers was taken to include all those who smoked regularly at the beginning of the pregnancy. In view of the findings by Butler & Goldstein mentioned above and since those who stopped smoking during pregnancy in this series were also known to be on average lighter smokers than those who continued, it was reasonable to exclude the 519 mothers who did not smoke after the second month of pregnancy, who formed about one fifth of the original group, in order to highlight the effects of maternal smoking. On the other hand, a separate analysis was also made of those who had only stopped smoking during the last three months of pregnancy, and even this subgroup showed similar figures for postneonatal mortality and morbidity up to the age of 5 to those of their controls (29).

In the choice of the controls great attention was paid to obtaining the best possible match with the study group in respect of the place of residence. This was done because one of the most prominent among the many differences between the smokers and non-smokers was the concentration of the smokers in the population centres, and in this extensive study area —160 000 km² (26)—the regional differences in childhood mortality and the use of the health care services are in many respects more important than the social class differences between the families (27, 28). Since the controls also had to be similar to the smokers in respect

of maternal age, parity, marital status and number of children born, it was not possible to set any additional demands for similarity between the groups. As seen from Tables 1, 2 and 5, the slightly different distribution into social groups among the smokers and controls did not affect the results.

The method of collecting the data on admissions to children's departments differed from that used for ascertaining admissions to any hospitals in the area or out-patient visits, the former being recorded directly from the hospital records and the latter two being collected by questionnaire from the child welfare centres. It is probable that in the latter two cases some under-estimation may exist, but this would affect the study group and controls similarly. The effects of regional differences were carefully eliminated when the control was chosen and the maternal smoking was not indicated in any phase of the follow-up study. 91.5% of the children in the northern province and 95.4% in the southern province were registered at a child welfare centre before the age of one in 1967 (23).

The studies most commonly referred to in which no adverse effect of maternal smoking on *perinatal mortality* is found are those of Järvinen & Österlund (15), O'Lane (17), Peterson et al. (25), Underwood et al. (37, 38), Yerusalmy (39, 40) and the present series (26). Sets of data showing that maternal smoking may also have an adverse effect on perinatal mortality have become more numerous, however, the best known investigations being those of Andrews & McGarry (1), Bailey (2), Butler et al. (3, 4) Comstock et al. (8, 9), Fabia (11), Russel et al. (32), Meyer et al. (19-21) and Rush & Kass (31).

In order to explain the contradictory findings on the effect of maternal smoking on perinatal mortality it has been suggested that smoking is more harmful to the infants of some groups of women than others (19, 20). In the Ontario Perinatal Mortality Study, Meyer et al. (20) found that the increased risk of perinatal mortality due to maternal smoking was

low if the mother was young, of low parity, non-anemic and smoked lightly, but high if the mother was of high parity, of public hospital status, had previous low birth-weight infants, or had a low hemoglobin level. Similarly Rush & Kass (31) found that black smokers had a perinatal mortality rate considerably higher than other groups, while among white mothers the effect of smoking was of lesser magnitude. In Washington County study (8) the higher mortality rate caused by maternal smoking was most marked among families who ranged low on socio-economic characteristics and the infants of primiparas and young mothers were less likely to suffer in this way.

Even though the lowering effect of maternal smoking on the birth weight in this series was clear (26, 29) the perinatal mortality was no higher among the smokers, and no clear trend for maternal smoking to be more injurious in the lower social groups was found (Table 1). One possible explanation for this deviant result is the small number of heavy smokers in the series and the fact that the smokers were in general young, low parity women (30).

The finding that maternal smoking increased *childhood mortality after the perinatal period* is similar to that of Comstock & Lundin (8), the two highest social groups being least affected (Table 2).

In contrast to the dissimilar findings concerning maternal smoking and perinatal mortality in different series, the few investigations made on the effect of maternal smoking in childhood morbidity mainly agree well, especially for children under one year of age.

In the study by Cameron et al. (5) based on telephone interviews with 727 Detroit metropolitan families it was found that the presence of tobacco smoke in the environment was associated with poorer physical health in children aged 16 or less, respiratory diseases being the most common causes of illness. Harlap & Davies (13) have investigated admissions to hospital in West Jerusalem infants during their first year of life, noting that the infants of mothers who smoked during pregnancy, 9.2%

of the total of about 10 000 interviewed, had significantly more admissions for respiratory diseases, especially in the winter, and more injuries than the infants of non-smokers. Colley et al. (7) and Leeder et al. (18) investigated 2 205 families in northwest London and found an association with parental smoking in the incidence of pneumonia and bronchitis under five, this finding being clearest for those under one year of age. Concerning the older children, the opposite has been reported in a couple of studies, Shy et al. (34) did not find any relationship between parents' smoking and respiratory diseases among second-grade school children, and in the study by Schilling et al. (33) the findings concerning children between the ages of seven and 18 were similarly negative, Kerrebijn et al. (16) also observed that smoking and non-smoking parents had about the same proportion of school-age children with respiratory symptoms. They also point out that if the respiratory symptoms of the smoking parents themselves were studied simultaneously it could be shown that it is more a question of the relationship between the symptoms of the parents and those of the children than between the tobacco smoke in the environment and the children's symptoms.

In this series a clearly higher number of [text obscured] The longer mean duration of hospital admissions among the children of smokers, a finding departing from that of Harlap & Davies (13), is most probably also an index of the higher degree of severity of their diseases. The higher diseases frequency in the chil-

dren of the smokers as calculated from the hospital admissions, was clearest in the case of respiratory diseases. [text obscured] effect of tobacco smoke in environment.

Concerning the diagnoses which were not the main causes of hospital admission but given during hospitalizations, it is difficult to judge if any real difference exists between the groups. It may be a question either of children taken into hospital for one reason being more likely to acquire other diagnoses more frequently than those not taken into hospital, or of children suffering from one disease being more prone to others. The latter is true, for example, in the case of iron deficiency anemia, the most common blood disease among Finnish children, for children with frequent or serious respiratory infections are also more disposed to this type of anemia. On the other hand, the lesser degree of significance is not necessarily a sign of a smaller difference between the groups, but may also reflect the smaller number of cases in the group, which is the case when only some of the hospital admissions are concerned.

The difference in respiratory diseases between the children of the smokers and of the controls was not so clear in the causes of visits to the doctor as in the causes of hospital admissions. Part of the explanation at least, may be found in the fact that the difference between the groups is clearest in the more severe diseases. However, the most frequent causes of out-patient visits among the children of the smokers were mainly found in the same diseases groups as in the diagnoses given in the children's departments (Table 6).

A clear dose-related effect under the age of one year was found both in the number of visits to the doctor and admissions to hospital.

and in the frequencies of the diseases, the children of heavy smokers being more seriously affected. The explanation for the fact that this was no longer true for children of the age of one to five may lie in the greater resistance of this age group, but also be related to the fact that maternal smoking habits were recorded only during the pregnancy and overlapping has occurred between the groups of heavy and light smokers and even between the smokers and non-smokers in the course of the years. On the other hand, the small number of heavy smokers in the series makes this group more easily effected by random variation than the five times larger group of light smokers.

In contrast to the study on Jerusalem infants by Harlap & Davies (13), no clear trend was found in this series for hospital admission caused by maternal smoking to be more frequent in winter. Part of the explanation, at least, may lie in the fact that the healthiest period for Finnish children is not exactly identical with the summer months, but is located on average during later summer and early autumn, May and June still being quite busy times in pediatric practise.

Maternal smoking was recorded during pregnancy and not later. Moreover, most mothers who do not stop smoking during pregnancy did not do so later. This is discussed more fully in another context (29). Paternal smoking was not recorded in this study, as is the case with most mother–child studies. However, mothers spend more time at home on average than do fathers, especially during their children's early years and, on the other hand, it is obvious that it will not be any more common for the father to smoke in families where the mother does not than in those whose she does.

In order to explain the differences found between the children of the smokers and the controls the following hypotheses can be presented. First, it can be assumed that even if the controls were chosen as carefully as possible from the five times larger group of non-smokers, they would not differ from these only

in their smoking habits, but in several other respects, e.g. in their biological characteristics, in their manner of taking care of their own health and that of their children, in their dietary habits, frequency of breast-feeding, and so on. In fact, some doubts are still expressed as to whether any true causal relationship exists between maternal smoking and increased perinatal mortality or reduced birth weight (10, 12, 35). At the same time, however, Goldstein (12) has shown that: "Various attempts to falsify the causal hypotheses have failed, leaving us with good reason for acting as if smoking really did cause a decrease in birthweight and an increased risk of perinatal mortality."

If we accept the causal theory also in respect of the later childhood period, we still have to judge which is more important, the foetal period or the infancy period. For the diseases in which the children of the smoker differed most from the others in this series, the respiratory and skin diseases, it seems reasonable that the smoke in the environment should be most important. However, the importance of other contributing factors such as lower birth weight has not yet been analysed thoroughly.

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as well as dyspnoea is higher in smokers than it is in nonsmokers and it is also higher in the inhabitants of Vlaardingen than it is in those of Vlagtwedde. The $FEV_{1.0}$ showed few differences between smokers and nonsmokers and between the inhabitants of Vlaardingen and those of Vlagtwedde.

Conclusion

The data currently available in the literature on the relationship between air pollution and the incidence of respiratory disease are not in accord with one another. This is due, among other things, to the fact that it is difficult to adequately differentiate between the effect of concurrent other provocative factors and that of air pollution The relationship between air pollution and meteorological factors or the climate interferes with many studies on the short-term effects of air pollution. In certain weather conditions which may induce respiratory symptoms (such as the concurrent presence of fog, a calm and sunlight), pollutant particles will not be dispersed but will continue to float over a particular area so that it will be hard to determine which is the (main) cause of an increase in respiratory symptoms. The problems relating to this matter have been described by Cassell et al. (4), among others.

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APPENDIX V. EFFECT OF PARENTAL SMOKING ON
RESPIRATORY SYMPTOMS IN THEIR CHILDREN

Various studies have been conducted on the effects of parental smoking on respiratory symptoms in children.

Cameron (1) made a telephone inquiry into the relationship between disease during the week prior to the inquiry and smoking by members of the family in 1 000 families in Denver. The number of patients among smokers and nonsmokers was equal in individuals over nineteen. In those under nineteen, the proportion of patients in smoking families was larger than that in nonsmoking families.

Cameron et al. (2) carried out a similar telephone inquiry on smoking habits and disease in 1 000 families in Detroit. They learned that respiratory disease was more common in 0-16-year-old children of smoking families than it was in children of nonsmoking families. This difference was not statistically significant in children under five. The amount of smoke to which the children were exposed in smoking families of sick children was larger than it was in smoking families in which the children were not ill.

Norman-Taylor (3) studied the relationship between respiratory infection and parental smoking habits in five-year-old children. In nonsmoking families, 33.5 per cent of the children showed respiratory symptoms. In those families which included heavy smokers (one or several individuals smoking over twenty cigarettes daily), this proportion was 44.5 per cent.

Colley (4) examined the relationship between coughing in children in the 6 to 14 year range and parental smoking habits. The number of coughing children was smallest in nonsmoking parents and largest when the two parents smoked. Independently of parental smoking habits, there was a definite relationship between respiratory symptoms in the parents (in which expectoration on arising was adopted as a cri-

terion) and constant coughing in the children. The number of coughing children of smoking parents without respiratory symptoms was only slightly larger than that of nonsmoking parents without respiratory symptoms. The results were obtained by questionnaires completed by the parents.

Colley et al. (5) did follow-up studies in 2 205 children in North-West London; the studies started in the first year of life and were continued over a five-year period. Inquiries were made each year regarding pneumonia and bronchitis in the children and smoking habits and respiratory symptoms in the parents. During the first year of life, there was a relationship between the symptoms shown by the children and parental smoking. Bronchitis and pneumonia were more common in children of smoking parents than they were in children of nonsmoking parents. This relationship was absent in children after the first year of life. On the other hand, there was a correlation between respiratory symptoms in the parents (expectoration on arising being adopted as a criterion) and bronchitis and pneumonia in the children. In the first year of life, the hazard of bronchitis and pneumonia in the children was doubled by parental smoking.

O'Connell et al. (6) studied the effect of cigarette-smoke on asthma in children. For this purpose, a group of asthmatic patients was compared with a group of controls. Sixty per cent of the parents of the patients were smokers, as was also the case with 60 per cent of the parents of the controls. Smoke caused aggravation of the asthma in 26 per cent of the patients whose parents did not and in 67 per cent of those whose parents did smoke. In the controls smoke was experienced as an irritant of the respiratory tract by 2 per cent of the children whose parents

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did not and by 16 per cent of those whose parents did smoke. Of the asthmatic children of non-smoking parents, 2 per cent showed an exacerbation of symptoms after inhaling cigarette smoke. This was the case with 16 per cent of the asthmatic children who had a single smoking parent and with 20 per cent of those who had two smoking parents. A considerable proportion of those asthmatic children whose symptoms were aggravated by cigarette smoke showed fewer symptoms when the parents gave up smoking.

Harlap et al. (7) did a prospective study of the number of admissions during the first year of life in children of mothers with known smoking habits. Children of smoking mothers were hospitalized more frequently than were those of non-smoking mothers. Admissions for bronchitis and pneumonia were significantly more common in children of smoking mothers than they were in children of nonsmoking mothers. This was only found to be the case with children from 6 to 9 months of age.

CONCLUSION

The studies of the relationship between parental smoking and respiratory disease in children showed that:

(1) The effect of parental smoking on respiratory symptoms in children cannot be considered without paying attention to parental symptoms. A differentiation should be made between the effect of parental respiratory symptoms on the children through genetic factors and cross infection and the effect of cigarette smoke.

(2) Symptoms of asthma induced in children by smoke are aggravated more often when the parents are smokers than when they are non-smokers.

(3) The degree of sensitivity to cigarette smoke probably varies with age.

(4) The amount of smoke inhaled has an effect on the symptoms.

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APPENDIX VI. TABLES 1-26

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Table 1. Sick absence,[a] comparison of chronic and acute conditions, The Netherlands, 1966, 1963, 1958

	Numbers of I.S.C.[b]	1966 % of total number of days of absence	Average duration per spell of absence (days) M	Average duration per spell of absence (days) F
Chronic diseases				
Cardiovascular diseases	410-416			
Diseases of endo-myo- or pericardium	420-422, 430-432	6.9	167.1	129.1
Disturbances in rate and rhythm	434	0.3	68.2	68.2
Other heart diseases		0.3	104.2	78.3
Hypertension and arteriosclerosis		2.6	114.4	89.2
Other diseases of the arteries		0.6	139.1	69.6
Total		10.7	118.6	86.9
Respiratory diseases	502, 526			
Chronic bronchitis emphysema, bronchiectasis	241, 317, 0, 510, 512, 522,	4.0	73.7	29.7
Asthma	525, 527, 583	1.5	42.4	32.6
Other chronic respiratory diseases (excluded pneumoconiosis)	(783.0 excl.)	1.1	20.5	17.6
Total		6.6	45.5	26.6
Chronic arthritis and arthrosis	722-725	5.6	102.2	112.2
Ulcer of stomach and duodenum	540-542	5.0	55.5	55.6
Displacement of intervertebral disc	735	4.3	95.8	103.6
Acute diseases				
Psychoneurotic disorders	310-314, 317, 5, 318, 354, 780, 6, 790, 791	16.8	34.4	30.3
Respiratory diseases	051, 470-475, 480-483, 490-493, 500, 501, 511, 783, 0	34.4	11.8	10.0
Gastrointestinal diseases (excl. appendicitis)	048, 049, 543, 544, 570, 571, 576	7.2	14.2	12.0
Accidents	742, N800-N999	13.7	24.6	25.9

[a] Insured population of Trade Associations.
[b] I.S.C. International Statistical Classification of Diseases Injuries and Causes of Death.

1963			1958		
% of total number of days of absence	Average duration per spell of absence (days)		% of total number of days of absence	Average duration per spell of absence (days)	
	M	F		M	F
7.3	152.8	145.5	6.2	138.4	125.7
0.3	63.9	50.9	0.3	56.1	49.9
0.3	88.7	56.5	0.2	60.3	67.0
2.6	113.9	92.1	2.5	106.5	92.1
0.5	115.8	31.8	0.4	112.9	41.6
11.0	107.0	75.4	9.6	94.8	75.3
4.3	75.9	30.6	3.8	58.7	23.4
1.9	43.1	32.9	2.5	34.9	26.6
0.9	23.0	18.5	0.9	24.6	17.0
7.1	47.3	27.3	7.2	39.4	22.3
5.6	93.1	105.9	6.1	92.2	98.5
5.0	54.5	51.6	7.2	53.6	54.2
4.5	83.1	97.9	5.3	79.3	94.7
13.8	31.2	27.4	10.7	26.6	24.5
37.5	13.1	10.4	37.8	11.7	9.9
7.6	14.1	11.7	6.2	13.0	11.2
14.4	25.4	26.1	11.4	23.6	23.7

Table 2. *Mortality from asthma[a] and chronic bronchitis[b], males and females, per 100 000 of each age group, 1959-1971, the Netherlands*

From: The International Statistical Classification of Diseases, Injuries and Causes of Death.

Year	Age (years)	
	< 20	20-39
1959	0.2	1.1
1960	0.2	1.4
1961	0.2	1.0
1962	0.2	0.9
1963	0.2	1.2
1964	0.2	1.1
1965	0.2	1.1
1966	0.3	0.9
1967	0.3	1.7
1968	0.2	1.0
1969	0.3	1.1
1970	0.1	0.4
1971	0.3	0.6

[a] Number 241 (-1968), 493 (1969+).
[b] Number 491 (-1968), 502 (1969+).

Table 3. *Attendance rate, 1968-1972*

Year	Attendance popul. A[a] (%)	Attendance popul. B[a] (%)
1968	70.6	
1969	90.4	75.0
1970	92.0	85.4
1971	98.2	97.5
1972	94.0	96.2
All years	58.3	60.0

[a] Attendants are equally divided over areas, birth cohorts and sexes.

Table 4. *Number and percentage of positive and negative answers, per question*

Question (1968)	Hoogvliet, Number 622			IJsselmonde, Number 630		
	Yes	No	Un-known	Yes	No	Un-known
3. Did your child cough like this on most days for as much as three or more months a year?	46 (7)	573 (92)	3	45 (7)	584 (93)	1
4. Did your child cough like this on most days in winter for as much as three or more consecutive months?	24 (4)	595 (96)	3	19 (3)	611 (97)	
5. Did your child cough like this on most days in summer for as much as three or more consecutive months?	6 (1)	613 (99)	3	3 (1)	627 (99)	

In parenthesis: in % of total.

Table 5. *Answer to question 36a (1968), 47a (1969). (Did your child ever suffer from eczema), 1968-1969*

Group	p	P	π	Number investigated
1-1[a]	0.051	0.004	0.019	274
1-3[b]	0.025	0.004	0.060	241
2-1	0.084	0.005	0.033	203
2-3	0.087	0.027	0.034	237

[a] In 1968 interviewer 1, in 1969 interviewer 1
[b] In 1968 interviewer 1, in 1969 interviewer 3, etc.

Table 6. *Answer to question 36e (1968), 47e (1969). (Have the tonsils been removed), 1968-1969*

Group	p	P	π	Number investigated
1-1[a]	0.535	0.008	0.079	275
1-3[b]	0.569	0.004	0.107	241
2-1	0.598	0.000	0.049	204
2-3	0.524	0.013	0.064	237

[a] In 1969 interviewer 1, in 1969 interviewer 1.
[b] In 1968 interviewer 1, in 1969 interviewer 3, etc.

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Table 7. *Reproducibility of histamine thresholds (mg/ml), 1968-1970*[a]

1968	1969		
	≤8	16 + ≥ 32	Total number
≤8, mg/ml	6	4	10
16 + ≥32, mg/ml	12	184	196
Total number	18	188	206

1968	1970		
	≤8	16 + ≥ 32	Total number
≤8, mg/ml	2	8	10
16 + ≥32, mg/ml	1	166	167
Total number	3	174	177

1969	1970		
	<8	16 + > 32	Total number
≤8, mg/ml	7	48	55
16 + ≥32, mg/ml	3	661	664
Total number	10	709	719

[a] Measurements in May-June of each year.

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Table 8. *Number of children investigated, according to birth cohort, sex and symptom group, 1968–1972 (population A)*
Dyspnoea+, Cough+, c+w+n+: see text page 15

Birth cohort	Sex	Dyspnoea+ Cough+	Dyspnoea+ Cough-	Dyspnoea- Cough+	Dyspnoea – Cough –								Un-known	Total
					c+w+ n+	c+w- n+	c+w+ n-	c+w- n-	c-w+ n+	c-w- n+	c-w+ n-	c-w- n-		
1968														
1/10/60	M	6	13	8	6	6	5	5	2	29	4	130	0	214
30/9/61	F	1	11	9	3	2	0	9	1	22	3	152	1	214
Total		7	24	17	9	8	5	14	3	51	7	282	1	428
1/10/55	M	2	13	0	1	3	1	2	1	19	2	145	1	190
30/9/56	F	2	6	4	0	1	2	2	0	18	3	161	0	199
Total		4	19	4	1	4	3	4	1	37	5	306	1	389
Total general		11	43	21	10	12	8	18	4	88	12	588	2	817
In % of total general		1.3	5.3	2.6	1.2	1.5	1.0	2.2	0.5	10.8	1.5	71.9	0.2	100
1969														
1/10/60	M	2	19	4	2	4	3	4	4	20	10	141	1	214
30/9/61	F	0	16	4	1	5	1	10	0	23	3	151	0	214
Total		2	35	8	3	9	4	14	4	43	13	292	1	428
1/10/55	M	2	24	0	0	2	1	2	1	13	4	141	0	190
30/9/56	F	3	25	0	0	5	0	4	1	15	2	143	1	199
Total		5	49	0	0	7	1	6	2	28	6	284	1	389
Total general		7	84	8	3	16	5	20	6	71	19	576	2	817
In % of total general		0.9	10.3	1.0	0.3	2.0	0.6	2.4	0.7	8.7	2.3	70.6	0.2	100
1970														
1/10/60	M	3	23	2	2	2	1	4	4	24	6	143	0	214
30/9/61	F	3	10	1	0	5	2	2	4	24	6	157	0	214
Total		6	33	3	2	7	3	6	8	48	12	300	0	428
1/10/55	M	3	23	1	1	1	0	7	1	17	5	129	2	190
30/9/56	F	0	18	0	1	3	0	2	1	20	5	149	0	199
Total		3	41	1	2	4	0	9	2	37	10	278	2	389
Total general		9	74	4	4	11	3	15	10	85	22	578	2	817
In % of total general		1.1	9.1	0.5	0.5	1.3	0.3	1.8	1.2	10.4	2.7	70.9	0.2	100

1971

1/10/60	M	5	20	3	1	1	2	5	5	15	7	146	4	214
30/9/61	F	2	17	1	1	8	3	3	1	13	2	163	0	214
Total		7	37	4	2	9	5	8	6	28	9	309	4	428
1/10/55	M	1	19	1	1	2	1	3	0	10	5	144	3	190
30/9/56	F	0	27	1	0	7	1	3	1	12	1	144	2	199
Total		1	46	2	1	9	2	6	1	22	6	288	5	389
Total general		8	83	6	3	18	7	14	7	50	15	597	9	817
In % of total general		1.0	10.2	0.7	0.3	2.2	0.9	1.7	0.9	6.1	1.8	73.1	1.1	100

1972

1/10/60	M	3	16	4	1	3	0	1	6	15	9	153	3	214
30/9/61	F	0	11	3	2	3	0	3	2	17	6	163	4	214
Total		3	27	7	3	6	0	4	8	32	15	316	7	428
1/10/55	M	2	12	3	0	2	0	2	2	10	8	149	0	190
30/9/56	F	0	19	2	0	5	1	1	1	15	0	150	5	199
Total		2	31	5	0	7	1	3	3	25	8	299	5	389
Total general		5	58	12	3	13	1	7	11	57	23	615	12	817
In % of total general		0.6	7.1	1.5	0.3	1.6	0.1	0.9	1.3	7.0	2.8	75.3	1.5	100

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Table 9a. *Number and percentage of children with cough, breathlessness on exertion, asthmatic attacks, rhinitis, according to birth cohort, 1968–1972 (population A)*

In parenthesis: % of total number. Total numbers differ because of unknown or unreliable answers in some items

Year	Birth cohort 1/10/60–30/9/61				Birth cohort 1/10/55–30/9/56			
	Age	Pos.	Neg.	Total	Age	Pos.	Neg.	Total
1. Cough · 3 months a year[a]								
1968	6/7	52 (12.1)	376	428	11/12	17 (4.3)	372	389
1969	7/8	27 (6.3)	401		12/13	8 (2.0)	381	
1970	8/9	19 (4.4)	409		13/14	12 (3.0)	377	
1971	9/10	18 (4.2)	407		14/15	11 (2.8)	378	
1972	10/11	15 (3.5)	412		15/16	14 (3.6)	375	
2. Cough, ≥ 3 consecutive months, in winter and/or summer[b]								
1968	6/7	24 (5.6)	400	424	11/12	8 (2.0)	375	383
1969	7/8	9 (2.1)	415		12/13	5 (1.3)	378	
1970	8/9	9 (2.1)	415		13/14	4 (1.0)	379	
1971	9/10	11 (2.6)	413		14/15	3 (0.7)	380	
1972	10/11	10 (2.3)	414		15/16	7 (1.8)	375	

3. Cough, 1 and 2 consecutive months, in winter and/or summer[c]

Year	Age	1 month	2 months	Total	Age	1 month	2 months	Total
1968	6/7	—	—	—	11/12	—	—	—
1969	7/8	37 (8.6)	19 (4.4)	428	12/13	17 (4.3)	8 (2.0)	389
1970	8/9	30 (7.0)	14 (3.2)		13/14	26 (6.6)	7 (1.8)	
1971	9/10	38 (8.8)	21 (4.9)		14/15	21 (5.4)	7 (1.8)	
1972	10/11	22 (5.1)	11 (2.5)		15/16	19 (4.8)	9 (2.3)	

4. Dyspnoea on exertion in winter and/or summer[d]

Year	Age	Pos.	Neg.	Total	Age	Pos.	Neg.	Total
1968	6/7	17 (4.0)	407	424	11/12	17 (4.4)	368	385
1969	7/8	36 (8.4)	388		12/13	52 (13.5)	333	
1970	8/9	38 (8.9)	386		13/14	43 (11.1)	342	
1971	9/10	45 (10.6)	379		14/15	47 (12.2)	338	
1972	10/11	27 (6.3)	397		15/16	31 (8.0)	354	

5. Asthmatic attacks, in winter and/or summer[e]

Year	Age	Pos.	Neg.	Total	Age	Pos.	Neg.	Total
1968	6/7	16 (3.7)	410	426	11/12	12 (3.1)	374	386
1969	7/8	2 (0.4)	424		12/13	7 (1.8)	379	
1970	8/9	3 (0.7)	423		13/14	5 (1.3)	381	

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Table 9 a (continued)

	Birth cohort 1/10/60–30/9/61				Birth cohort 1/10/55–30/9/56			
Year	Age	Pos.	Neg.	Total	Age	Pos.	Neg.	Total
1971	9/10	3 (0.7)	423		14/15	3 (0.7)	383	
1972	10/11	5 (1.1)	421		15/16	1 (0.2)	385	
6. Rhinitis, in winter and/or summer[f]								
1968	6/7	52 (12.3)	370	422	11/12	18 (4.6)	366	384
1969	7/8	42 (9.9)	380		12/13	17 (4.4)	367	
1970	8/9	41 (9.7)	381		13/14	22 (5.7)	362	
1971	9/10	36 (8.5)	386		14/15	13 (3.4)	371	
1972	10/11	26 (6.1)	396		15/16	23 (5.9)	361	

[a] Affirmative answers to one or more of questions 3 (1968); 5, 7 (1969).
[b] Affirmative answers to one or more of questions 4, 5 (1968); 6, 9 (1969).
[c] Affirmative answers to one or more of questions 7, 8, 10, 11 (1969).
[d] Affirmative answers to one or more of questions 15, 16, 17 (1968); 15, 16, 17, 18, 19, 20 (1969).
[e] Affirmative answers to one or more of questions 24 (1968); 27, 29 (1969).
[f] Affirmative answers to one or more of questions 29 (1968); 34, 38 (1969).

Table 9 b. Number and percentage of children in symptom-positive groups, 1968–1972 (population A)
In parenthesis: % of total number.

		Boys			Girls			Boys + girls		
Year	Age (years)	Pos.[a]	Neg.[b]	Total	Pos.[a]	Neg.[b]	Total	Pos.[a]	Neg.[b]	Total
Birth cohort 1/10/1960–30/9/1961										
1968	6/7	27 (12.6)	187	214	21 (9.8)	193	214	48 (11.2)	380	428
1969	7/8	25 (11.6)	189		20 (9.3)	194		45 (10.5)	383	
1970	8/9	28 (13.1)	186		14 (6.5)	200		42 (9.8)	386	
1971	9/10	28 (13.1)	186		20 (9.3)	194		48 (11.2)	380	
1972	10/11	23 (10.7)	191		14 (6.5)	200		37 (8.6)	391	
Birth cohort 1/10/1955–30/9/1956										
1968	11/12	15 (7.9)	175	190	12 (6.0)	187	199	27 (6.9)	362	389
1969	12/13	26 (13.7)	164		28 (14.1)	171		54 (13.9)	335	
1970	13/14	27 (14.2)	163		18 (9.0)	181		45 (11.6)	344	
1971	14/15	21 (11.1)	169		28 (14.1)	171		49 (12.6)	340	
1972	15/16	17 (8.9)	173		21 (10.6)	178		38 (9.8)	351	

[a] D + C +, D + C −, D − C +: see text p. 15.
[b] Unknown included.

Table 9c. Percentage of children with cough, breathlessness on exertion, asthmatic attacks, rhinitis, and in symptom positive groups according to age (population A)

Age (years)	Cough > 3 months a year	Cough > 3 consec. months a year	Cough 2 consec. months a year	Cough 1 consec. month a year	Dyspnoea on exertion	Asthmatic attacks	Rhinitis	D + C+ D + C− D − D+ [a]
6/7	12.1	5.6	—	—	4.0	3.7	12.3	11.2
7/8	6.3	2.1	4.4	8.6	8.4	0.4	9.9	10.5
8/9	4.4	2.1	3.2	7.0	8.9	0.7	9.7	9.8
9/10	4.2	2.5	4.9	8.8	10.6	0.7	8.5	11.2
10/11	3.5	2.3	2.5	5.1	6.3	1.1	6.1	8.6
11/12	4.3	2.0	—	—	4.4	3.1	4.6	6.9
12/13	2.0	1.3	2.0	4.3	13.5	1.8	4.4	13.9
13/14	3.0	1.0	1.8	6.6	11.1	1.3	5.7	11.6
14/15	2.8	0.7	1.8	5.4	12.2	0.7	3.4	12.6
15/16	3.6	1.8	2.3	4.8	8.0	0.2	5.9	9.8
Number 6/11	428	428	428	428	424	426	422	428
Number 11/16	389	389	389	389	385	386	384	389
Total number all ages	817	817	817	817	809	812	806	817

[a] See text p. 15.

Table 10a. Number and percentage of children, according to the number of years with a positive item, per item and birth cohort (population A)

In parenthesis: % of total number. Total numbers differ because of unknown or unreliable answers in some items.

Number of years positive	Cough[a] Birth cohort 1/10/60–30/9/61				Birth cohort 1/10/55–30/9/56			
	> 3 months a year	> 3 consec. months a year	2 consec. months a year	1 consec. month a year	> 3 months a year	> 3 consec. months a year	2 consec. months a year	1 consec. month a year
0	344 (80.3)	381 (89.0)	405 (94.6)	374 (87.4)	346 (88.9)	370 (95.1)	377 (96.9)	345 (88.6)
1	54 (12.6)	33 (7.7)	21 (4.9)	49 (11.4)	31 (7.9)	14 (3.6)	12 (3.0)	38 (9.7)
2	17 (3.9)	12 (2.8)	2 (0.4)	2 (0.4)	7 (1.8)	4 (1.0)	0	5 (1.3)
3	10 (2.3)	1 (0.2)	0	3 (0.7)	4 (1.0)	0	0	0
4	2 (0.4)	1 (0.2)	0	0	0	0	0	1 (0.2)
5	1 (0.2)	0			1 (0.2)	1 (0.2)		
Total number	428	428	428	428	389	389	389	389

[a] Criteria see Table 9a.

Table 10b. Number and percentage of children according to number of years with symptoms,[a] birth cohort and sex (population A)

Number of years positive	Birth cohort 1/10/60–30/9/61						Birth cohort 1/10/55–30/9/56					
	Boys		Girls		Boys + girls		Boys		Girls		Boys + girls	
	N	%	N	%	N	%	N	%	N	%	N	%
0	154	71.9	167	78.0	321	75.0	146	76.8	150	75.4	296	76.1
1	30	14.0	23	10.7	53	12.4	17	8.9	20	10.0	37	9.5
2	9	4.2	13	6.1	22	5.1	8	4.2	14	7.0	22	5.6
3	8	3.7	5	2.3	13	3.0	8	4.2	3	1.5	11	2.8
4	6	2.8	5	2.3	11	2.6	6	3.2	10	5.0	16	4.1
5	7	3.3	1	0.5	8	1.9	5	2.6	2	1.0	7	1.8
Total	214	100	214	100	428	100	190	100	199	100	389	100

[a] D ÷ C÷, D + C–, D – C÷: see text p. 15.

	Dyspnoea on exertion[a]		Asthmatic attacks[a]		Rhinitis[a]	
	Birth cohort		Birth cohort		Birth cohort	
	1/10/60–30/9/61	1/10/55–30/9/56	1/10/60–30/9/61	1/10/55–30/9/56	1/10/60–30/9/61	1/10/55–30/9/56
	344 (81.1)	300 (77.9)	401 (94.1)	371 (96.1)	330 (78.2)	329 (85.6)
	39 (9.2)	34 (8.8)	23 (5.4)	10 (2.6)	39 (9.2)	36 (9.3)
	17 (4.0)	20 (5.2)	1 (0.2)	1 (0.2)	23 (5.4)	8 (2.0)
	10 (2.3)	13 (3.3)	0	1 (0.2)	16 (3.8)	5 (1.3)
	10 (2.3)	13 (3.3)	1 (0.2)	2 (0.4)	6 (1.4)	4 (1.0)
	4 (0.9)	5 (1.3)	0	1 (0.2)	8 (1.9)	2 (0.5)
	424	385	426	386	422	384

[a] Criteria see Table 9a.

Table 11. *Number and percentage of children according to symptoms and previous history (population A)*

Positive answer on question[a]		Cough >3 months a year				Cough >3 consecutive months a year				Cough 2 consecutive months a year				Cough 1 consecutive months a year			
		1–5×		0×		1–5×		0×		1–4×		0×		1–4×		0×	
		N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%
36h ('68)	178	62	48.8	116	16.7	37	56.1	141	18.8	14	40.0	164	21.0	44	44.9	134	18.7
36i ('68)	308	103	81.1	205	29.8	58	87.8	250	33.4	23	65.7	285	36.5	56	57.1	252	35.1
36j ('68)	83	21	16.5	62	9.0	11	16.7	72	9.6	5	14.2	78	10.0	20	20.4	63	8.8
19 ('68)	206	65	51.2	141	20.5	38	57.6	168	22.4	17	48.6	189	24.2	39	39.8	167	23.3
12 ('69)	138	61	48.0	77	11.2	37	56.1	101	13.5	14	40.0	124	15.9	34	34.7	104	14.5
21 ('69)	115	47	37.0	68	9.9	33	50.0	82	10.9	10	28.6	105	13.5	27	27.6	88	12.3
28 ('69)	27	14	11.0	13	1.9	8	12.1	19	2.5	3	8.6	24	3.1	8	8.2	19	2.6
30 ('69)	22	11	1.6	7	10.6	15	2.0	3	8.6	19	2.4	6	6.1	16	2.2	16	2.2
Total number	815	127		688		66		749		35		780		98		217	

[a]
36h (1968) Did your child ever have periods of asthma or bronchitis?
36i (1968) Did your child ever have periods of cough?
36j (1968) Did your child ever have pneumonia?
19 (1968) Did your child ever wheeze?
12 (1969) Did your child ever have periods of cough for as much as 3 consecutive months in the previous years?
21 (1969) Has your child ever been troubled by shortness of breath when playing outdoors or walking up a staircase in the previous years?
28 (1969) When resting did your child ever have attacks with shortness of breath in winter in the previous years?
30 (1969) When resting did your child ever have attacks with shortness of breath in summer in the previous years?

Kerrebijn, K.F., Hoogeveen-Schroot, H.C.A., van der Wal, M.C.
"Chronic Nonspecific Respiratory Disease In Children, A Five-Year
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SUMMARY: Asthma, chronic bronchitis and emphysema (chronic
nonspecific respiratory disease, CNSRD) are common conditions in
adults (32,34) and children (29) in the Netherlands. Many children
with symptoms belonging to the CNSRD syndrome will continue to
have these into adult life[1] (3,9,17,21,23,42,44,53,54). The various
studies concerning the history of CNSRD in childhood are hardly
comparable as regards their design and results. The definitions
of asthma, asthmatic bronchitis, recurrent bronchitis and chronic
bronchitis in children and the criteria for recovery or improvement
are not sufficiently clear. Recent and previous symptoms are often
not differentiated. The critical evaluation of the effect of
treatment on the course of the disease is insufficient in most
studies.

In the majority of children , the symptoms of CNSRD begin
in the first five years of life. The chance that they will persist
into adulthood seems to be least in those children, in whom symptoms
are not frequent or slight and disappear during school age. Some
findings suggest that optimum treatment and favourable psychosocial
conditions have a beneficial effect on the course of the disease.
However, to quantitate these is difficult.

It will therefore often be impossible to make a reasonable
prediction of the prognosis of CNSRD in childhood for adult life.
In order to ensure optimum curative and preventive medical care,
it will be essential to examine the conditions in which the
injurious effects of exogenous factors, such as allergens,
infections, chemical and physical agents and unfavourable
psychosocial circumstances, are reduced to a minimum. However,
studies on the relative significance of various exogenous factors
are difficult to perform. These studies are merely practicable in
homogeneous, clearly defined populations living under specific
conditions in which only a limited number of exogenous factors
play a role.

In view of the morbidity of CNSRD, the most extensive
possible preventive care in addition to optimum treatment of signs
and symptoms is essential. Among others, this will include
counselling of smokers, vocational guidance, advice on housing,
etc. This is of importance in adults and, to an even greater
extent, in subjects in the 10-20 year range, in whom adequate health
care and health counselling will contribute to a favourable course.
In adults morbidity and absenteeism due to CNSRD would
presumably be considerably reduced if children running and increased
risk of CNSRD in later life could be selected at an early stage
and given adequate care.
This aspect, i.e. the selection of children running an
increased risk, is the subject of the present study.

CHRONIC NONSPECIFIC RESPIRATORY DISEASE IN CHILDREN, A FIVE YEAR FOLLOW-UP STUDY

BY

K. F. Kerrebijn, M.D., H. C. A. Hoogeveen-Schroot, M.D. and M. C. van der Wal, M.D.

CONTENTS

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1. INTRODUCTION

Asthma, chronic bronchitis and emphysema (chronic nonspecific respiratory disease, CNSRD) are common conditions in adults (32, 34) and children (29) in the Netherlands. Many children with symptoms belonging to the CNSRD syndrome will continue to have these into adult life[1] (3, 9, 17, 21, 23, 42, 44, 53, 54). The various studies concerning the history of CNSRD in childhood are hardly comparable as regards their design and results. The definitions of asthma, asthmatic bronchitis, recurrent bronchitis and chronic bronchitis in children and the criteria for recovery or improvement are not sufficiently clear. Recent and previous symptoms are often not differentiated. The critical evaluation of the effect of treatment on the course of the disease is insufficient in most studies.

In the majority of children, the symptoms of CNSRD begin in the first five years of life. The chance that they will persist into adulthood seems to be least in those children, in whom symptoms are not frequent or slight and disappear during school age. Some findings suggest that optimum treatment and favourable psychosocial conditions have a beneficial effect on the course of the disease. However, to quantitate these is difficult.

It will therefore often be impossible to make a reasonable prediction of the prognosis of CNSRD in childhood for adult life. In order to ensure optimum curative and preventive medical care, it will be essential to examine the conditions in which the injurious effects of exogenous factors, such as allergens, infections, chemical and physical agents and unfavourable psychosocial circumstances, ar reduced to a minimum. However, studies on the relative significance of various exogenous factors are difficult to perform. These studies are merely practicable in homogeneous, clearly defined populations living under specific conditions in which only a limited number of exogenous factors play a role.

In view of the morbidity of CNSRD, the most extensive possible preventive care in addition to optimum treatment of signs and symptoms is essential. Among others, this will include counselling of smokers, vocational guidance, advice on housing, etc. This is of importance in adults and, to an even greater extent, in subjects in the 10-20 year range, in whom adequate health care and health counselling will contribute to a favourable course.

In adults morbidity and absenteeism due to CNSRD would presumably be considerably reduced if children running and increased risk of CNSRD in later life could be selected at an early stage and given adequate care.

This aspect, i.e. the selection of children running an increased risk, is the subject of the present study.

2. EPIDEMIOLOGY OF CNSRD

2.1. PREVALENCE

For the literature on the prevalence of CNSRD in the Netherlands and other countries, the reader is referred to the thesis by Van der Lende (31) and a number of papers published by the TNO Working group on the Epidemiology of CNSRD (33, 34).

[1] A detailed review of this literature is available at the author.

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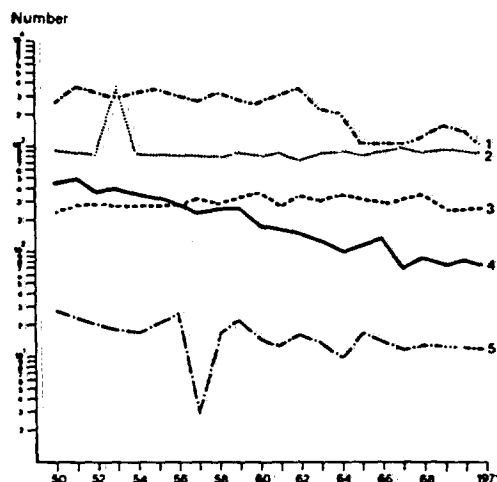
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Fig. 1. Deaths by congenital malformations (1) (numbers 750–759 (– '68), 740–759 ('69 ↔)), accidents (2) (numbers E800–E999), neoplasms (3) (numbers 140–239), pneumonia (4) (numbers 490–493 (– '68), 480–486 ('69 ↔ 1)), and chronic non specific lung diseases (5) (numbers 241, 502, 526, 527.1 (– '68), 493, 391, 518, 492 ('69 ↔), boys and girls, 0–14 years of age, 1950–1971, The Netherlands. Numbers of the international statistical classification of diseases, injuries and causes of death.

2.2. ABSENTEEISM DUE TO SICKNESS

Table 1 shows absenteeism due to a number of chronic and acute conditions in the Netherlands in 1958, 1963 and 1966. More recent data have not been published.

Among the chronic conditions, chronic respiratory disease (mainly CNSRD) is the next important cause of absenteeism after cardiovascular disease. Absenteeism was estimated at from 10 000 to 11 000 man years in 1966.

The considerable social significance of acute respiratory conditions which cause five times the absenteeism due to chronic respiratory disease is accentuated by the table. It should be pointed out that it is not impossible but even likely that part of the absenteeism resulting from acute respiratory conditions occurs in cases of chronic respiratory disease and is directly due to the latter. The figures reported for chronic respiratory disease as the cause of absenteeism are therefore likely to be minimum figures.

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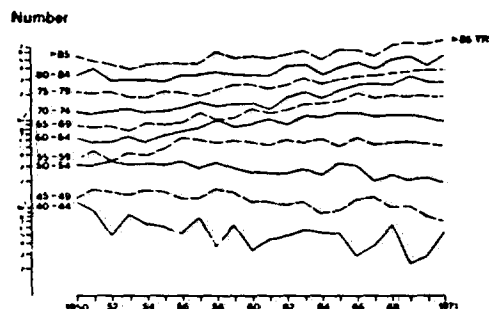
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Fig. 2. Mortality from chronic nonspecific lung diseases (numbers 241, 502, 526, 527.1) (– '68), 493, 491, 518, 492 ('69 ↔)), males, per 100 000 of each age group, 1950–1971, The Netherlands. Numbers of the international statistical classification of diseases, injuries and causes of death.

2.3. MORTALITY

In 1968, Speizer (47) and his associates published mortality rates from asthma in a number of countries. These showed a marked increase in subjects in the 10–19 year range in Great Britain, Japan and Australia. It was suggested that this could have been due to the excessive use of aerosol bronchodilators and the fact that administration of steroids during exacerbations was inadequate.

Table 2 shows the death rates from asthma and chronic bronchitis in subjects in the 0–39 year range per 100 000 of each age group in the Netherlands. The rates are very low and there was no increase during the period from 1959 to 1971.

The difference in mortality rates between the
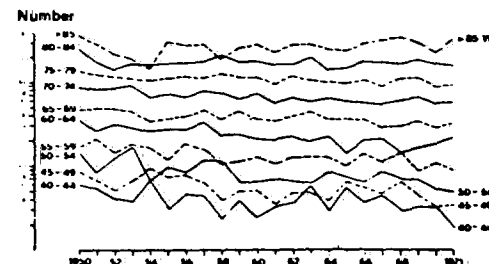
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Fig. 3. Mortality from chronic nonspecific lung diseases (numbers 241, 502, 526, 527.1 (– '68), 493, 491, 518, 492 ('69 ↔)), females, per 100 000 of each age group, 1950–1971, The Netherlands. International statistical classification of diseases, injuries and causes of death.
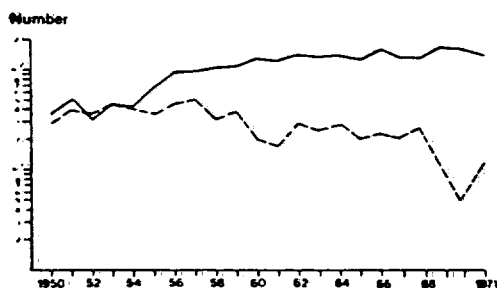
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Fig. 4. Deaths by chronic bronchitis and emphysema, —, (numbers 502 + 527.1 (− '68) 491 + 492 ('69 −)) and asthma, ---, (numbers 241 (− '68), 493 ('69 +)), males, 55–59 years of age, 1950–1971, The Netherlands. Numbers of the international statistical classification of diseases, injuries and causes of death.

Number

Fig. 5. Mortality from chronic bronchitis and emphysema (numbers 502 resp. 527.1 (− '68), 491 resp. 492 ('69 −)) compared to mortality from arteriosclerotic heart disease (numbers 420 (− '68), 410, 411, 412, 413, 414 ('69 +)), men (— —) and women (--- —), 50–54 years of age, The Netherlands. Numbers of the international statistical classification of diseases, injuries and causes of death.

Netherlands and Great Britain is hard to account for, particularly as the clinical picture and general schedules of treatment are comparable in the two countries.

In Figure 1, the number of subjects in the 0–14 year range who died from CNSRD is compared with the number of deaths from congenital malformations, accidents, neoplasms and pneumonia. These figures also show that CNSRD is a minor cause of death in children.

Figures 2 and 3 show the mortality from CNSRD per 100 000 men and women over forty. Mortality is higher in men than it is in women. The men show an increase from the 55th year of life. This begins about the year 1954. The increase is caused by chronic bronchitis and emphysema, as is apparent from Figure 4. (This figure is concerned with subjects in the 55–59 year range; it also holds true, however, for the older age groups.) The cause of this increase is obscure. Increased cigarette smoking may possibly be a factor. An outstanding feature is the fact that the mortality from bronchitis and emphysema runs parallel to that from cardiovascular disease, although absolute mortality is lower. This is illustrated in Figure 5 for those in the 50–54 year range.

3. STUDY DESIGN AND OBJECTIVES

From 1968–1972 a follow-up study on symptoms and signs of CNSRD was performed in randomly selected populations of schoolchildren in Rotterdam.

The aim was to investigate the appearance or disappearance of symptoms of CNSRD and to select children running an increased risk of CNSRD in adult life by means of a standardised questionnaire. This was supplemented by pulmonary function tests, determination of the bronchial reactivity, allergy skin tests, chest radiography and investigations about social factors, air pollution, parental smoking habits and parental respiratory symptoms.

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4. POPULATIONS STUDIED

4.1. In 1968, this consisted of:

(1) 175 boys and 175 girls born during the period from October 1960 to October 1961 and living in the Hoogvliet district.

(2) 175 boys and 175 girls born during the period from October 1955 to October 1956 and living in the Hoogvliet district.

(3) 175 boys and 175 girls born during the period from October 1960 to October 1961 and living in the IJsselmonde district.

(4) 175 boys and 175 girls born during the period from October 1955 to October 1956 and living in the IJsselmonde district.

The total number was 700 children of Hoogvliet and 700 children of IJsselmonde. *This population will henceforth be referred to as population A.* These were randomly selected populations taken from children born during the above periods and living in Hoogvliet and IJsselmonde on October 1, 1967. They were chosen for the following reasons:

(1) Clinical experience has shown that changes in the occurrence of symptoms of CNSRD can be expected in the 6–16 year range.

(2) The two districts are newly constructed areas with favourable housing and social conditions.

(3) Industrial air pollution was greater in the Hoogvliet district than it was in the IJsselmonde district at the beginning of the study.

4.2. As it was advisable to increase the number of children with symptoms in view of the follow-up, 255 children of the relevant cohorts, who were recorded as having symptoms of CNSRD by the school medical officers and living in Hoogvliet and IJsselmonde, were selected in 1969. The findings in these children were used only in longitudinal studies and not in data on prevalence. *This population will be further referred to as population B.*

4.3. The numbers and proportions of children of populations A and B who fully took part in the study during the period from 1968 to 1972 are listed in Table 3. In each year, the children are equally distributed over the districts and sexes; the number of those of the older cohort taking part is slightly smaller than is that of those of the younger cohort. (The difference was approximately 10 per cent in 1972.) The reasons for not taking part were traced wherever possible by home visits or telephone calls. Although specific inquiries were made in this regard, respiratory symptoms were not stated as the reason in any of these cases. Change of residence was the reason in approximately one-third of those who did not take part in the study during the period from 1969 to 1972; the other most often stated reasons were:

— objections to committing oneself to a five-year period
— objections on schoolabsence
— objections on principle
— inadequate interest in the study
— family reasons
— severe mental or physical disorders in the child to be studied
— refusal on the part of the child.

5. METHODS OF INVESTIGATION

5.1. QUESTIONNAIRES ON SYMPTOMS

5.1.1. General

A European Coal and Steel Community (ECSC) questionnaire modified for children was used in taking the medical histories of the children. In 1968, the histories concerned the last two years; in the next few years, they only concerned the year just ended. The questions were asked by two investigators (physicians). In 1968,

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the parents were sent a questionnaire in advance with the request to complete it at home. The questions asked in the questionnaire were broadly similar to those asked during the investigation. This self-administered questionnaire was designed to prepare the parents for the questions that would be asked during the investigation. It was regarded as essential that the answers should reflect reality wherever possible, i.e., that the methods adopted in this study should discriminate as sharply as possible. For this reason, the original ECSC questionnaire was modified to some extent as early as 1968. Specifically the following passage was included orally in questions 1-3 after "usually": "that is to say, as many as five days a week on average". Moreover questions 4 and 5 were added, in which it was explicitly stated what was meant by "three months a year", namely, three *consecutive* months a year. Table 4 shows that this makes a considerable difference in the number of affirmative answers. The questionnaire was extended with questions on cough for two months and one month in 1969. Therefore the numbering of the questions had to be changed in 1969. It is already indicated in the text and the tables to which year the numbering of a question refers. The questionnaire is given in Appendix 1.

5.1.2. *Reliability of the questionnaire*

(1) The answers to question 36 *h* (1968) ("Did your child ever have any attacks of bronchitis or asthma?") were compared with those to questions on cough, dyspnoea and asthmatic attacks. All children examined were classified into one of four symptom groups (dyspnoea + cough + (D + C +) dyspnoea + cough - (D + C -) dyspnoea - cough + (D - C +) dyspnoea - cough - (D - C -). For details, see Section 6.1, p. 15). This comparison did not justify any doubt as to the correctness of the answers to the questions used in classifying the children into symptom groups.

(2) It was checked whether children showing symptoms of CNSRD which were severe enough

for referral to the outpatient department of the respiratory unit of the Sophia Children's Hospital, always were classified into one of the symptom-positive groups after their parents had answered the questionnaire. This was done in 76 children. Independently another investigator attempted to answer the questionnaire using the children's hospital records.

The difference between and similarity of the answers to each question in the records and questionnaire have been recorded. Fifty-nine percent of the answers were identical in the records and questionnaire, whereas this was not the case with twenty-seven percent. Fourteen percent of the answers were not reliable.

The similarity was found to be most marked in questions relating to the previous histories of the subjects. In view of the background of the children, this is an obvious finding. Cough was less frequently coded in the affirmative according to the questionnaire than it was according to the records. The similarity of the questions on dyspnoea was fairly close.

Conclusion. In the children showing respiratory symptoms, there is inadequate similarity between the findings in the questionnaire and those in the records as regards the symptom cough and fairly adequate similarity where the symptom dyspnoea is concerned. The questionnaire shows an underreporting of the symptom cough.

(3) A number of the variables included in the study, such as cough and dysponoea, are marked by dichotomy of the values, i.e., they show whether a particular symptom has or has not occurred or whether it is present. Efforts were made to study the variations in frequency distribution of such a variable from one survey to another. The following parameters were introduced for this purpose.

p = possibility in errors of coding
P = possibility of appearance of the symptom with which the question is concerned at the time of the first survey

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π = possibility of the symptom having occurred during the interval between the first and second surveys.

The values of p, P and π about the variables "history of eczema" (question 47a (1969)) and "tonsils removed" (question 36e (1968)) have been estimated by the maximum likelihood method. This was done separately in four groups. These groups differed from one another in that they were questioned by different interviewers in at least one of the two years during which inquiries were conducted. These questions are best suited to verify the reproducibility of the result obtained, as a finding which was positive in 1968 should continue to be so during the following years. The calculated estimates of the values of p, P and π are shown in Tables 5 and 6. The groups in these tables are composed according to the numbers of the successive interviewers; group 1-3 for instance, includes those children who were interviewed by interviewer 1 in 1968 and interviewer 3 in 1969.[1]

The tables show that the estimated value of p (the percentage of faulty codings) continues to be very low. It is highest in group 2-3.

(4) In fifty children of the oldest birth cohort, the questionnaires were separately submitted to the mother and the child at several weeks' intervals. The similarity between the answers given on the two occasions ranged from good to excellent.

(5) As is apparent from Tables 12 and 13, the mean one-second forced expiratory volume $(FEV_{1.0})$ and the mean forced expiratory volume expressed as a percentage of the vital capacity $(FEV_{1.0}\%)$ of children with dyspnoea on exertion are significantly lower than those in children showing no respiratory symptoms (D·C−, c w n) (for further explanation of these tables, see p. 18).

Conclusion drawn from studies on the reliability of the questionnaire. The answers to the ques-

tions asked in the questionnaire appear to be fairly reliable and readily reproducible. Appreciable differences between interviewers were not observed. Comparison of the results obtained using the questionnaire with the findings in the records of the out-patient department is not possible. A small proportion of the out-patients to whom the questions of the questionnaire were put were classified with the group in which symptoms were absent. This was probably due to the fact that treatment had reduced the symptoms to such an extent in these cases that they no longer satisfied the criteria adopted for the groups in which symptoms were present. This may, naturally, also be the case in population surveys and may result in an unduly low symptom prevalence rate. The symptom most difficult to evaluate is dyspnoea on exertion. The $FEV_{1.0}\%$ of children who showed only this symptom is significantly lower than that in nondyspnoeic subjects, which supports the reliability of the indicative value of this question. Appendix II includes a review of the literature on observer's errors.

5.2. SOCIAL QUESTIONNAIRE

In 1969 and 1970, the homes of all children who had taken part in the entire survey in 1969 were visited. A questionnaire on social and demographic data was completed by a health visitor trained for this work. If required, she explained the purpose of the survey in greater detail and also urged people to continue taking part in it to the best of their ability. This data was collected for the purpose of obtaining information on the social and demographic backgrounds of the children under investigation and their families.

5.3. QUESTIONNAIRE ON THE STATE OF HEALTH OF PARENTS, BROTHERS AND SISTERS

In 1972, the parents were sent a questionnaire for the purpose of collecting data on the family background of respiratory symptoms and smoking habits (36).

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[1] In 1969, interviewer 3 took the place of interviewer 2 who had to discontinue her activities because of change of residence.

5.4. PHYSICAL EXAMINATION

The upper and lower respiratory tract were physically examined each year. In addition, the height, weight and physical development were measured by standardized methods (39, 48).

5.5. FUNCTION TESTS

Pulmonary function tests were performed and the histamine threshold was determined each year. This was done in population A from 1968 in the oldest and from 1969 in the youngest cohort and in population B from 1969. Pulmonary function tests were invariably performed between the end of April and mid-June to avoid accidental diminution because of respiratory symptoms due to seasonal factors as much as possible. They were only performed when no respiratory symptoms were present at the time of investigation.

5.5.1. Pulmonary function tests

The following values were determined:

(1) In all children the vital capacity (VC) and one-second forced expiratory volume ($FEV_{1.0}$) using a Lode water sealed spirometer (model D53).

(2) In a limited number of randomly selected children of each birth cohort, the total lung capacity and the residual volume by means of the He method, using a volumograph no. 4 (Mijnhardt).

5.5.2. Histamine threshold

The reactivity of the bronchi was determined by the histamine threshold (52) using the expiratory peak flow instead of the VC and FEV_1 as parameters of bronchial obstruction. The expiratory peak flow was measured with a Wright peak-flow meter.

5.5.2.1. Comparison of the histamine threshold as measured with the spirometer and with the Wright peak-flow meter. In 327 children (those taking part in the population survey as well as children attending the out-patient department of the respiratory unit of the Sophia Children's Hospital), the histamine threshold was determined by the spirometer and by the

Wright peak-flow meter. The results of the two methods of determination were in good agreement.

5.5.2.2. Reproducibility of the histamine threshold. In Table 7, the number of children of population A in whom various determinations of the histamine threshold were carried out during the period from 1968 to 1970 are listed. Normal or slightly lowered histamine thresholds ($16 + \geqslant 32$ mg/ml) are readily reproducible; markedly lowered thresholds ($\leqslant 8$ mg/ml) often show an improvement.

5.5.2.3. Relationship between initial pulmonary function and histamine thresholds. This was studied in a separate survey (Appendix III). This study showed that there is some relationship between the initial $FEV_{1.0}$ or the peak flow and the histamine threshold. When the histamine threshold is known, however, it is not possible to even approximately predict the $FEV_{1.0}$, nor can the histamine threshold be predicted when the $FEV_{1.0}$ is given. Repeated measurements of pulmonary function and the histamine threshold showed that these often show an opposite trend (i.e. histamine threshold decreases and pulmonary function increases or vice versa).

Conclusion. The determination of the histamine threshold as a parameter of the bronchial reactivity seems to be useful in addition to the measurement of the pulmonary function. These two quantities are probably largely determined by different factors. The histamine threshold is readily reproducible in the normal and slightly lowered range when it is measured over a number of years. It would be of major importance to know whether a histamine threshold which is permanently lowered (i.e., also during an optimum clinical period in which the VC and $FEV_{1.0}$ are within normal limits) his any significance for the prognosis.

5.6. ALLERGY TESTS

Tests for cutaneous allergy to house dust, mixed moulds,[1] grass pollen[2] and danders[3] were

[1] The mixed moulds included: Trichoderma viride, Fusarium culmorum, Cladosporium, Cladosporiades, Cladosporium elatum, Cladosporium herbarum, Rhizo-

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performed in population A in 1968 and in population B in 1969. Testing with house dust, grass pollen and danders could be repeated in a number of children in the spring of 1973 after the main study had been completed, by the same technicians.

The allergens used were Diephuis allergens at the following concentrations: intracutaneous injection of 0.5 mg/ml of house dust and, in the case of a positive reaction, additional injection of 0.05 mg/ml and 0.005 mg/ml; intracutaneous injection of 0.2 mg/ml of mixed moulds and when a positive response was obtained, additional injection of 0.02 mg/ml and 0.002 mg/ml; intracutaneous injections of 1 000 Noon units of grass pollen and, for positive reactors, additional injection of 100 Noon units and 10 Noon units; intracutaneous injection of 0.25 mg/ml of danders and, in the event of a positive response, additional injection of 0.025 mg/ml and 0.0025 mg/ml.

The allergens used in 1973 were of the same batch as those used during previous years. They had been stored in the freeze-dried state.

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pus nigricans, Stemphylium botryosum, Alternaria tenuis, Penicillium brevi compactum, P. expansum, P. notatum, P. frequentans, P. commune, Aspergillus versicolor, Aspergillus niger, Aspergillus fumigatus, Mucor sponosus, Mucor mucedo, Mucor racemosus, Pullularia pullulans, Botrytis cenerea, Merculius domesticus, Epicoccum purparascens.

The grass pollen included: Secale cereale (rye), Dactylis glomerata (cocksfoot grass), Lolium perenne (rye-grass), Anthoxantum odoratum (sweet vernal grass), Alopecurus pratensis (meadow foxtail grass), Agrostis alba (white bent), Holcus lanatus (Yorkshire fog), Cynosurus cristatus (crested dogtail).

Human and animal danders: Man, horse, swine, cat, goat, cattle, rabbit, dog, sheep and various birds.

To study the repeatability of the tests for cutaneous allergy in individuals showing a positive response, skin testing was repeated in a number of asthmatic patients of the Sophia Children's Hospital with positive intracutaneous reactions. These patients were treated but had not been desensitized. The technicians performing the skin tests were not aware of the results of the previous tests. The repeatability was, on the whole, highly satisfactory in those age groups in which the present study was carried out.

5.7. RADIOGRAPHY

5.7.1. *Radiography of the lungs*

In 1968, X-rays of the lungs were made in all children of population A and, in 1969, in all those who were studied in population B. These X-rays were read by H. A. van Geuns, M.D., without knowing the children or their medical histories. He used a standardized method in which particular attention was paid to the lung pattern and hili.

5.7.2. *Determination of bone age*

X-rays of the left hand of all children were taken each year to determine the bone age in order to correlate this with height growth, development of puberty and pulmonary function. In each case, the bone age was determined by the same investigator (H.H.-S) using Tanner's method (49).

6. RESULTS

6.1. CLASSIFICATION INTO SYMPTOM GROUPS

For a convenient arrangement of the results, the following classification into symptom groups was made. It was based on the *major symptoms* of CNSRD i.e. prolonged cough, dyspnoea on

exertion and attacks of asthma (Text-table 1).

A classification into four symptom groups was based on the scheme: $D+C+$, $D+C-$, $D-C+$ and $D-C-$.

In the rating dyspnoea +, questions 15 and 24 of 1968 and questions 15, 18, 27 and 29 of

Text-table 1. *Classification into symptom groups based on major symptoms*

Dyspnoea	Questions 24 (1968), 27 and/or 29 (1969): When resting did your child ever have attacks of shortness of breath with wheezing at rest (asthmatic attacks)?	Questions 15 (1968), 15 and/or 18 (1969): Has your child ever been troubled by shortness of breath when playing outdoors or walking up a staircase?
D+	Yes	Yes
	Yes	No
	No	Yes
D-	No	No
Cough	Question 4 (1968) Question 6 (1969) Did your child cough like this[a] on most days in winter for as much as three or more consecutive months?	Question 5 (1968) Question 9 (1969) Did your child cough like this[a] on most days in summer for as much as three or more consecutive months?
C+	Yes	Yes
	Yes	No
	No	Yes
C-	No	No

[a] i.e. continuously, that is on average 5 days a week.

1969 were combined, as it is difficult to adequately differentiate between dyspnoea on exertion and dyspnoea at rest in children.

The D-C-group was subdivided into on the basis of "secondary" symptoms (Text-table 2).

6.2. PREVALENCE OF COUGH, DYSPNOEA ON EXERTION, ASTHMATIC ATTACKS AND RHINITIS IN POPULATION A

Table 8 includes a summary for each year of investigation, based on the birth cohort and sex per symptom group. In Table 9a, the number and percentage of children according to the year of investigation and the age of the children are listed for each symptom and birth cohort.

In Table 9b, this was done for the combination of symptom-positive groups (D+C+, D+C-, D-C+) per birth cohort and sex. The percentages listed in Tables 9a and 9b are summarized in Table 9c, having been arranged by age. The number and percentage of children in whom a particular symptom was present for 0, 1, 2, etc., years are stated in

Table 10a. The number and percentage of children classified in one of the symptom-positive groups for 0, 1, 2, etc., years are shown in Table 10b.

The following can be deduced from these tables:

(a) The total number of children taking part for five years consisted of 428 of the youngest group (61.1 percent of the initial number) and 389 of the oldest group (55.6 percent). As is

Text-table 2. *Subdivision of D-C-groups*

Cough	Wheezing	Nasal catarrh	Codes in tables
+	+	+	c+w+n+
+	-	-	c+w-n-
+	+	-	c+w+n-
+	-	+	c+w-n+
-	+	-	c-w+n-
-	-	+	c-w-n+
-	+	+	c-w+n+
-	-	-	c-w-n-

c(ough) : affirmative answer to questions 1 and/or 2 and/or 3 (1968): questions 1 and/or 2 and/or 3, and/or 4 and/or 5 (1969).
w(heezing) : affirmative answer to question 19 (1968); questions 23 and/or 25 (1969).
n(asal catarrh) affirmative answer to questions 29 and/or 30 (1968); 34 and/or 35-37, and/or 38, and/or 39-41 (1969).

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Text-table 3. *Number and percentage[a] of those taking part, 1968-1970*

Year	Birth cohort	
	1960-1961	1955-1956
1968	632 (90.2)	620 (88.5)
1969	495 (70.7)	467 (66.7)
1970	466 (66.5)	439 (62.7)
1971	441 (63.0)	410 (58.5)
1972	428 (61.1)	389 (55.6)

[a] 700 = 100 %.

apparent from Text-table 3, the largest proportion dropped out after the first survey. There was an equal sex distribution.

(b) In the youngest birth cohort, the number of boys included in any of the symptom-positive groups is larger than the number of girls in each year of investigation. The boy-girl ratio in the youngest birth cohort averages 3:2 (Tables 9a and 9b). In the oldest birth cohort, the number of boys in the symptom-positive groups in 1969, 1971 and 1972 is slightly smaller than is the number of girls, the boy-girl ratio averaging 1:1 in this cohort.

(c) *Coughing over prolonged periods* (three or more months a year or three or more consecutive months a year) is most common in six-year-old children (5.6 percent) (Tables 9a and 9c). In the older age groups, prolonged coughing occurs in only 1-2 percent of the cases, but coughing for three or more months a year is almost twice as common. It should be pointed out that the question asked in 1968 was concerned with prolonged coughing "in the past two years", so that affirmative answers to this question will partly refer to symptoms present at an age of four or five.

(d) The prevalence of *coughing for two consecutive months* is higher than is that of coughing for three or more consecutive months but lower than that of coughing for three or more months a year. The prevalence of coughing for one month is approximately twice as high as that of coughing for two months (Tables 9a and 9c). The number of children coughing for two consecutive months or for one consecutive month shows a marked decrease after the 9th-10th year of life.

(e) During the period of life in which the children start smoking (see also p. 26), the prevalence of coughing does not increase.

(f) *Dyspnoea.* The symptom "dyspnoea on exertion" shows a marked increase up to roughly 10 percent in the two birth cohorts during 1969 and the following years, whereas the incidence of asthmatic attacks drops to approximately 1 percent or less (Tables 9a and 9c). This might be partially accounted for by the fact that more effective treatment was instituted as a result of the initial survey, so that genuine attacks of asthma were less common and dyspnoea on exertion became the more outstanding feature. A large proportion of children predisposed to asthma are known to show exercise-induced bronchial obstruction even when the asthma is adequately controlled and attacks no longer occur (20, 24, 30). Unfortunately, this finding could not be verified, as it was not usually possible to obtain a clear picture of the effect of treatment on the course of the symptoms.

(g) The prevalence of *rhinitis*, like that of coughing for a short period, decreases after the 9th-10th year of life and occurs then in approximately 6 percent.

(h) As is apparent from Table 9b, the proportion of children classified into any of the *three symptom-positive groups* varies from approximately 9 to 12 percent in each age group, with exceptions downwards in the 11-12 year range and upwards in the 12-13 year range. These must be assumed to have been due by chance. A striking feature is the fact that no decrease occurs at the age of puberty. The number of children in whom a similar symptom is present in two or more of the five years of investigation is relatively small (Table 10a). Among the answers to the questions on cough "three months a year" is most common for

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several years, followed by "three consecutive months a year". Coughing for two consecutive months or for one month is only occasionally listed more than once. Among the respiratory symptoms listed in this table, dyspnoea on exertion is most frequently described as having been present for several years.

As was previously apparent from Tables 9*a* and 9*c*, Table 10*a* shows that the prevalence of cough is much lower in the oldest birth cohort than it is in the youngest. This also holds true for attacks of asthma and rhinitis but not for dyspnoea on exertion.

As is shown by Table 10*b*, approximately 2 percent of the children of the two birth cohorts belonged to one of the symptompositive groups for five consecutive years. This was the case with from 2 to 4 percent for four or three years.

Conclusions

(1) In most children showing symptoms of prolonged cough, dyspnoea or attacks of asthma, symptom shifts take place over the years. These are not reflected in the transversal prevalence rates.

(2) The symptom-positive groups—the prevalence of which does not vary markedly in the two birth cohorts during the various years of investigation—partly include a varying population. This means that a population of school-children characterized as "positive for CNSRD" in a transversal study may include individuals who will be found to not satisfy the classical criteria of CNSRD when follow-up studies are done in other years.

The reverse also is the case: Section 5.1.2.2. showed that children with recurrent respiratory symptoms are not invariably included in a symptom-positive group in transversal studies when the questionnaire is used in medical history-taking.

In order to gain a better understanding of the significance of these findings, the following relationships were studied:

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6.2.1. *The relationship between the frequency of a positive symptom and the previous history of respiratory symptoms*

The findings are shown in Table 11.

All symptoms are characterized by a marked, statistically significant ($P < 0.01$ chi-square test) similarity between their appearance in one or several years of investigation and an affirmative answer to questions regarding the previous history. As the number of cases in which a symptom is positive in more than two out of five years is small, it is difficult to decide whether a high incidence of symptoms is more frequently associated with a positive previous history than is a low incidence. This trend is un-doubtedly present

The similarity between prolonged cough, dyspnoea on exertion and attacks of asthma on the one hand and periods marked by cough on the other is a very striking feature. This is also the case with previous histories of children with dyspnoea on exertion, attacks of asthma and wheezing and the similarity between histories of attacks of asthma and cough.

Conclusion. There is a statistically significant relationship between respiratory symptoms in children at school age and those appearing in previous years.

6.2.2. *The relationship between respiratory symptoms and the pulmonary function parameters one-second forced expiratory volume ($FEV_{1.0}$) and the forced expiratory volume expressed as a percentage of the vital capacity ($FEV_{1.0}\%$).* (Tables 12 and 13)

The normal means shown in these tables for the $FEV_{1.0}$, i.e. the $FEV_{1.0}(E)$ were calculated from the findings in the children without recent respiratory symptoms ($D-C-, c-w-n-$) and with a negative previous history.

The mean $FEV_{1.0}\%$ was 81 ($\pm 10 = 2SE$). The figures listed in Table 13 were achieved by calculation of the mean pulmonary function values for each child from all measurements carried out during the course of the study. (Children in whom less than three measure-

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Text-table 4. *Analysis of variance of findings listed in Table 13*

Cough 3 months a year	Cough 3 consecutive months a year	Cough 2 consecutive months a year	Cough 1 month a year	Dyspnoea on exertion	Asthmatic attacks	Rhinitis	D+C+ D+C− D−C+	D−C− and/or n and/or w i	D−C− c−n−w
P = 0.01	P = 0.05	P = 0.05	P = 0.23	P < 0.01	P < 0.01	P = 0.01	P < 0.01	P = 0.37	P < 0.0

ments were made, were not included in the tables.) The averages were then calculated from the individual averages in each group. Comparison of the children with and without symptoms by age group (Table 12) shows that the mean $FEV_{1.0}\%$ is usually within one standard error of the normal mean ($\geqslant 76$ percent) for all symptoms with the exception of asthmatic attacks. Children having asthmatic attacks show a mean $FEV_{1.0}\%$ within two standard errors of the normal mean up to the fourteenth and fifteenth years of life; however the value decreases with increasing age. The mean $FEV_{1.0}\%$ is slightly lower in children with symptoms than it is in those without. This is particularly true for asthmatic attacks. Table 13 shows the mean $FEV_{1.0}\%$ according to the number of years during which a symptom was positive.

In the symptoms prolonged cough (three or more months a year, three or more consecutive months a year, two consecutive months a year), dyspnoea on exertion, attacks of asthma and rhinitis as well as in the symptom-positive combinations, the mean $FEV_{1.0}$ and mean $FEV_{1.0}\%$ decrease as the number of years in which the symptom or combination of symptoms was present, increase. This trend was verified by an analysis of variance (Text-table 4).

The trend is significant for all symptoms except cough during one consecutive month. The fact that the symptom-negative combination with positive "secondary" symptoms (D−C−, c and/or n and/or w +) does not show variations in pulmonary function indicates that the "secondary" symptoms are indeed of less importance than the major symptoms.

The fact that there is also a significant trend in rhinitis can be understood from Text-table 5, which shows that there is a relationship between the number of years in which rhinitis occurred and that in which other respiratory symptoms were present. This relationship is highly significant for all respiratory symptoms in this table ($P < 0.01$; chi-square test).

Conclusion. A study of the relationship between various respiratory symptoms and the number of years for which they were present shows that the pulmonary function parameters which were measured decrease with the duration of the symptoms.

This supports the view that these symptoms are relevant as parameters of recurrent or chronic respiratory disorders in children. The effect can be seen already in children who have a major symptom for only one year and it is most marked in children with asthmatic attacks. Prolonged cough, dyspnoea on exertion and the

Text-table 5. *Percentage of children with rhinitis associated with other respiratory symptoms*

Rhinitis (years) No. of years	Cough 3 months a year			Cough 3 consecutive months a year			Dyspnoea on exertion			Asthmatic attacks		
	0	1	≥ 2	0	1	≥ 2	0	1	≥ 2	0	1	≥ 2
0	90.0	8.3	1.7	97.1	2.3	0.6	34.1	8.3	7.6	95.3	4.1	0.6
1	50.0	31.3	18.8	62.5	30.0	7.5	57.5	16.2	26.3	87.5	8.8	3.3
≥ 2	58.2	11.4	30.4	73.4	15.2	11.4	46.8	21.5	31.6	88.6	6.3	5.1

symptom-positive combinations show a similar pattern in this regard. This means that the symptoms referred to must be taken into account in estimating risks, when they have appeared at least once at school age. (See also Section 7.4.)

6.2.3. *The relationship between respiratory symptoms and the histamine threshold*

This is shown in Table 14. Only those children in whom at least three determinations of the histamine threshold were made are included in this table. Each child is arranged in the order of frequency of the various symptoms according to the median value of all histamine thresholds determined in that child.

The question as to whether there is a relationship between the median histamine threshold value and the presence of respiratory symptoms was studied. The relationship between a markedly reduced median value of the histamine threshold (.8 mg/ml) and the presence of symptoms for one or several years is highly significant for each individual symptom and for the symptom-positive combinations (P .0.01, chi-square test). Because of insufficient numbers, this could not be examined for asthmatic attacks.

Conclusion. There is a statistically significant relationship between the presence of symptoms and a lowered histamine threshold. This also serves to support the relevance of the symptoms referred to as parameters of chronic or recurrent respiratory disorders in children. The question of whether a histamine threshold showing a permanent decrease has any prognostic significance (see also p. 24) cannot be answered because of the small number of children in whom this was the case. Follow-up studies in a selected population will be better suited for this purpose (26).

6.3. COMPARISON OF THE FINDINGS IN HOOGVLIET AND IJSSELMONDE IN RELATION TO AIR POLLUTION

Fig. 6 shows the mean monthly concentrations of sulphur dioxide and smoke in the two districts during the period from 1967 to 1972. As the determinations made in 1968 and the first half of 1969 were unreliable, these are not stated. Beginning in June 1969, air pollution was measured by a semiautomatic apparatus, the so-called merry-go-round. In view of the results of measurements in 1967 and previous years, it was believed that the concentrations of sulphur dioxide and smoke would be much higher in Hoogvliet than in IJsselmonde. However, a chimney which is 213 m high has come into use at the Shell refinery at Hoogvliet in 1969. The differences in air pollution between the two districts turned therefore out to be relatively slight after 1969.

In 1968, there was no appreciable difference in prevalence of symptoms between Hoogvliet and IJsselmonde. Also in the following years, there were no systematic or marked differences between the answers to the questions in the two districts. These answers therefore were not arranged by district in Tables 9–11.

For a summary of the most important literature on the subject of air pollution and respiratory disease, see Appendix IV.

6.4. ALLERGY TESTS

The results of the first and second series of skin tests are listed for each birth cohort in Table 15a.

The proportion of children of the two birth cohorts in whom the tests were positive showed a two- to threefold increase where house dust, grass pollen and danders were concerned. It comes as no surprise that the proportion of positive tests in the youngest birth cohort in 1973 is of the same order of magnitude as that in the oldest birth cohort in 1968 and 1969. In fifty percent of the children in whom skin tests were positive in both series, the positive test was associated with a lower allergen concentration in the second than it was in the first series. Table 15b shows the symptom pattern of the children in whom skin tests were positive in 1973 and that of those in whom all tests were negative.

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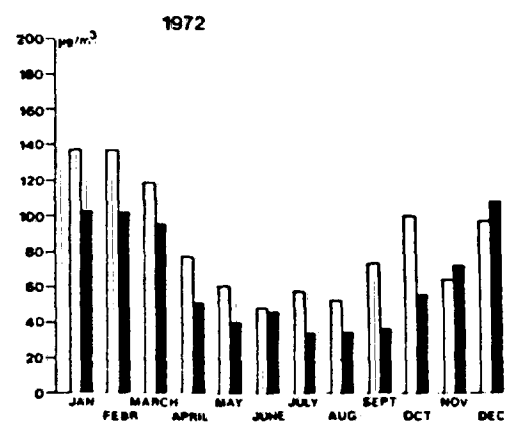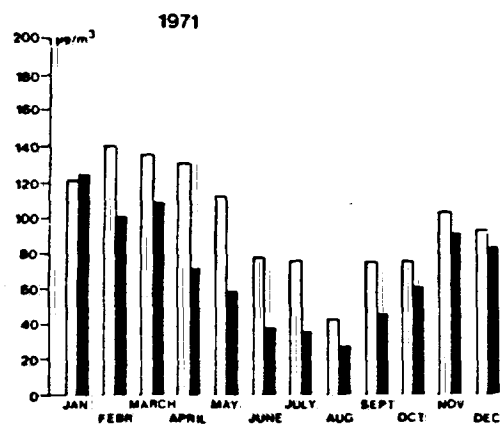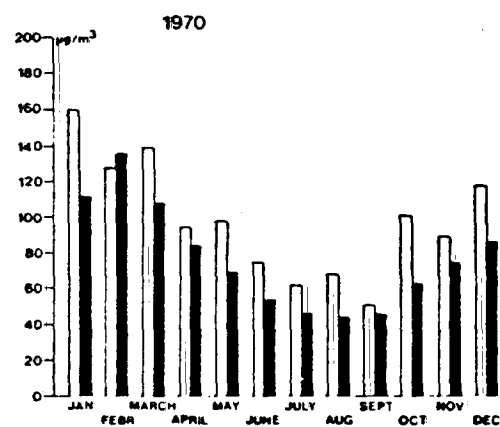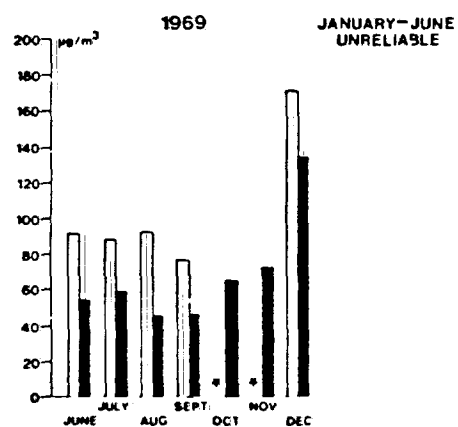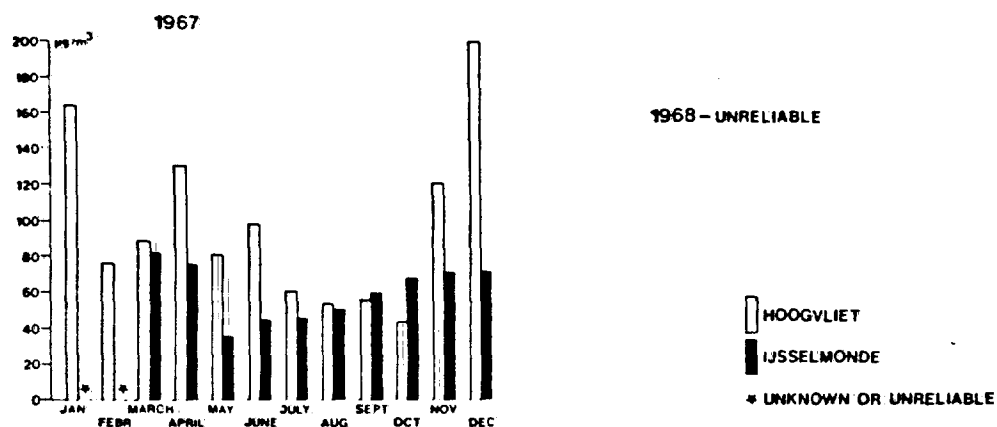
Fig. 6a. Mean concentrations of SO_2 ($\mu g/m^3$), Hoogvliet and IJsselmonde, 1967-1972.

1967

1968-UNRELIABLE

☐ HOOGVLIET

■ IJSSELMONDE

＊ UNKNOWN OR UNRELIABLE
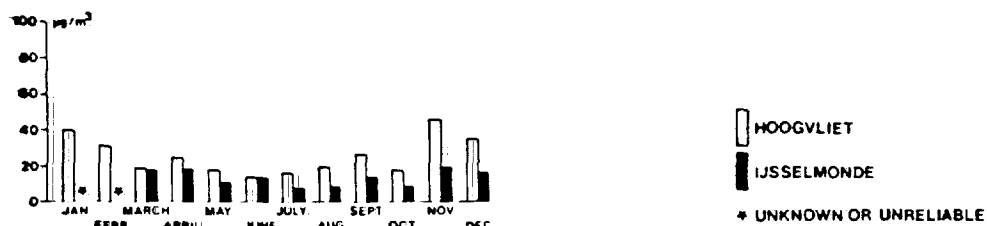
1969   JANUARY-JUNE
        UNRELIABLE

1970
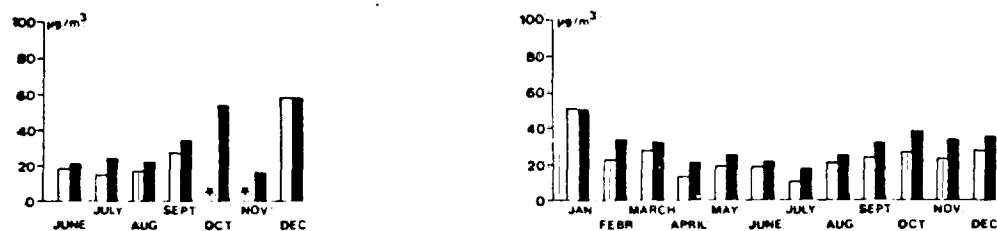
1971

1972
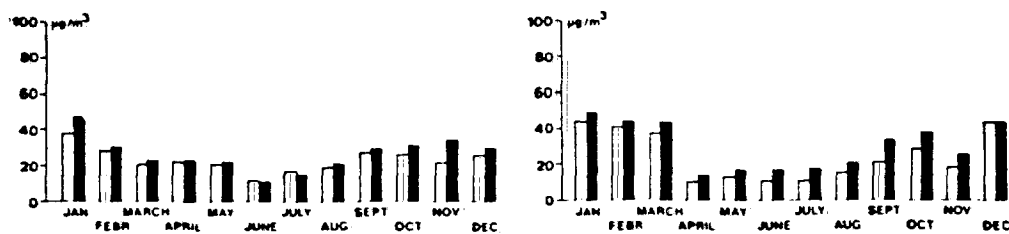
Fig. 6b. Mean concentrations of smoke ($\mu m/m^3$), Hoog-
vliet and IJsselmonde, 1967-1972.

Text-table 6. *P values of differences in symptom prevalence according to skin tests (chi-square test)*

Skin test	1973	1968/69	Cough > 3 months a year	Cough > 3 consec. months a year	Cough 1 and 2 consec. months a year	Dyspnoea on exertion	Rhinitis	D + C + D + C − D − C +
House dust	+ −		n.s.	n.s.	n.s.	$P = 0.02$	n.s.	$P = 0.04$
	+ +	+ −	n.s.	n.s.	n.s.	$P = 0.05$	n.s.	$P = 0.03$
Danders	+ −		$P < 0.01$	$P = 0.01$	$P = 0.1$	$P < 0.01$	$P < 0.01$	$P < 0.01$
	+ +	+ −	$P < 0.01$	n.s.	n.s.	$P < 0.01$	$P < 0.01$	$P < 0.01$

The children showing a positive response are arranged according to the allergen used and classified into a "first time negative – second time positive" group and a "twice positive" group.

The chi-square test was used to investigate the significance of differences in symptom-prevalence according to the skintests to house dust and danders[1] (Text-table 6).

Children in whom skin tests to house dust were positive in 1973 showed more often dyspnoea on exertion for one or several years and more often belonged to a symptom-positive group than children in whom skin tests were negative in 1973 ($P < 0.05$). This also was the case with children in whom skin tests to house dust were positive in 1973 and 1968/69 as compared with those in whom skin tests were positive in 1973 but negative in 1968–69 ($P < 0.05$).

Children in whom skin tests to danders were positive in 1973 had all symptoms more frequently than children in whom skin tests were negative in 1973 ($P < 0.01$). But in children with positive skin tests in 1973 and 1968/69 only cough for 3 or more months a year, dyspnoea on exertion and rhinitis were more prevalent than in those with positive tests in 1973 and negative in 1968/69 ($P < 0.01$).

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[1] Because of the small number of positives, significance tests have not been done for asthmatic attacks and grass pollen.

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Conclusion. An obvious relationship exists between the presence of respiratory symptoms and positive skin tests with house dust and danders. This relationship is most marked in the case of danders. This suggests that danders are of greater importance as an allergen than house dust in the population investigated.

A curious finding is the small difference between the proportion of children with positive skin tests to danders who live in households with and without domestic animals (18.0 and 15.6 percent respectively). These latter children obviously have contact with animals so often at school or at their friends' home that they yet become atopic.

6.5. RADIOGRAPHY

The number of children with increased line shadows and mottled shadowing is listed in Table 16. The two changes are mainly present in children of the symptom-negative group. Approximately 50 percent of the children with increased line shadows or mottling had a positive previous history.

Other radiological changes were observed in thirteen children. These consisted of:

— marked enlargement of the left hilus in one child. This child had a medical history which was negative for respiratory symptoms and showed a negative tuberculin test

— low diaphragm in four children

— a calcified area in the left upper field in one
child
— a broad mediastinal shadow in one child
— an azygos lobe in two children.

6.6. RELATIONSHIP BETWEEN SOCIAL AND DEMOGRAPHIC FACTORS AND RESPIRATORY SYMPTOMS

Housing conditions were favourable in the two districts. 54 percent of the children lived in a one-family house. Only 0.4 per cent of the houses were designated as inadequate. The proportion of houses containing one or several damp rooms was 10 percent. 62 percent of the children had their own bedroom, 32 percent shared their bedroom with one child, 6 percent shared it with two or more children. 71 percent of the families kept pets.

There existed no relationship between respiratory symptoms and the occupation of the father, the housing conditions except bedroom shared with two or more, and the presence of pets in the family.

6.7. RELATIONSHIP BETWEEN PARENTAL SMOKING AND RESPIRATORY SYMPTOMS IN CHILDREN

Table 17a shows the relationship between parental smoking and respiratory symptoms in the children in 1972.

Smoking and nonsmoking parents have about the same proportion of children with respiratory symptoms. The number of cigarettes smoked by the parents has no influence on respiratory symptoms in their children, as is shown in Table 17b.

These findings are in accordance with those reported by the majority of other investigators (Appendix V).

6.8. RELATIONSHIP BETWEEN RESPIRATORY SYMPTOMS IN PARENTS AND CHILDREN

Table 18a shows the relationship between respiratory symptoms in parents and children. The more symptoms the parents have, the more of their children belong to one of the symptom-positive groups ($P < 0.01$, chi-square test). Although this is the case in children of smokers and non smokers, it is most obvious in the smokers children, as is apparent from Table 19b.

6.9. LONGITUDINAL DATA FOR HEIGHT, SKELETAL MATURATION, WEIGHT AND PULMONARY FUNCTION

These will be published separately as soon as the statistical analysis has been completed.

DISCUSSION OF RESULTS

7.1. METHODS

As stated in Section 5.1.2, the answers to the questions posed in the *questionnaire* may be considered as sufficiently reliable for the calculation of prevalence data of respiratory symptoms in schoolchildren. The most common symptom which is the most difficult to evaluate is dyspnoea on exertion. An affirmative answer to the question "Has your child ever been troubled by shortness of breath when playing outdoors or walking up a staircase" (question 15 (1968), 15 and 18 (1969)) was adopted as a parameter, because question 14 (1968) ("Has your child ever been troubled by shortness of breath when cycling against the wind or on running?") was not considered to be sufficiently specific. The obvious relationship between a previous history of respiratory symptoms and an affirmative answer to this question (Table 11) and the fact that the mean pulmonary function values in children with dyspnoea on exertion were lower than those in children without respiratory symptoms (Tables 12 and 13) sug-

gests that an affirmative answer should be rated as such. This also holds true for the other major symptoms (cough for three or more consecutive months a year and asthmatic attacks) as well as for the questions cough for three or more months a year, cough for two consecutive months a year and rhinitis. The last three symptoms were included in symptom group $D-C-$ $(c+w-n+)$ to make a differentiation possible between the CNSRD group according to the widely accepted criteria based on studies in adults (36) and symptoms or combinations of symptoms which may be of importance earlier in life. Exercise-induced bronchial obstruction is a common symptom in children (20, 24, 30). Unfortunately, exercise tests using a treadmill or running to determine whether bronchial obstruction particularly occurs in the children with an affirmative answer to the questions on dyspnoea on exertion could not be performed.

Wheezing without prolonged cough, dyspnoea on exertion or asthmatic attacks does not affect pulmonary function. Wheezing has thererefore been classified among the minor symptoms.

Table 13 shows that the $FEV_{1.0}\%$ was a more sensitive parameter of *pulmonary function* than the $FEV_{1.0}$. This is in accordance with the findings reported by other investigators (22, 46). In children with symptoms the decrease in pulmonary function was slight and also in those with symptoms for many years, the mean $FEV_{1.0}\%$ usually was within one standard error of the normal mean in all symptoms with the exception of attacks of asthma. This can be partly due to the fact that—in order to obtain baseline values—measurements were carried out only when respiratory symptoms were not present at the time of investigation and in a season in which few respiratory infections occurred.

Future surveys should include pulmonary function tests revealing changes in the small bronchi, such as determination of the expiratory flow at small lung volumes and the closing volume (8, 16, 35, 40, 41, 55, 56).

Section 5.1.2. shows that *observer's errors*

(see also Appendix II) did not affect the answers to the questions to any appreciable extent. The reproducibility of the answers can be considered to be good. The *histamine threshold* is usually regarded as a measure of reactivity of the respiratory tract to nonspecific stimuli (43, 51) and as an endogenous characteristic of chronic nonspecific respiratory disease (52).

However, as de Vries (52) has shown, in adults the histamine threshold is dependent of the initial pulmonary function. As this relationship was rather weak in the children studied, we continued to determine the histamine threshold each year and we have considered it to be an independent characteristic of CNSRD (see also Appendix III).

Surveys for CNSRD showed that a relationship between respiratory symptoms and a lowered histamine threshold (≤ 16 mg/ml) was present in both adults (32) and children (29). The findings in children were verified by the present study.

As stated previously, measurements were carried out only when respiratory symptoms were absent at the time of investigation. This enhances the value of the relationship found to exist between the histamine threshold and a history of respiratory symptoms in regard to the relevance of these symptoms as parameters of chronic or recurrent respiratory disorders.

It is still questionable whether a lowered histamine threshold can be considered as an endogenous characteristic of CNSRD. Only 13 percent of the children in this study showed a diminished median histamine threshold (≤ 16 mg/ ml). This is too small a number to answer this question.

The prevalence of a lowered histamine threshold value varied considerably in the various years of investigation (Text-table 7).

This is more in favour of the histamine threshold to be a measure of the reactivity present at the time of investigation than to be an endogenous determined personal characteristic. This is also suggested by the findings in the Dutch alpine clinic for asthmatics in

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Text-table 7. *Annual prevalence of histamine threshold*

Year of investi- gation	Histamine threshold (mg/ml)		
	8 %	16 %	32 %
1968	5	14	81
1969	8	16	76
1970	1	9	90
1971	2	10	88
1972	4	7	89

Davos, where a lowered histamine threshold value is restored to normal levels in some patients, whereas it is not in others during their stay in the high mountains (25, 26).

Patients were examined for the presence of *allergy* by intracutaneous skin tests in which various concentrations of allergen were used as recommended by Voorhorst (50). Some investigators claim that it is preferable to perform skin tests on the back, as the results obtained by this method are believed to be more sensitive and more readily reproducible. This, however, is denied by others (19).

For psychological reasons, the present tests were performed on the volar surface of the right forearm. We used the intracutaneous method since this is more sensitive than the prick test and since the test can be performed with various concentrations of a particular allergen. The fact that reagins to a specific allergen are present in the skin does not imply that bronchial obstruction will occur on inhalation of the allergen (1, 28, 37).

In this survey we found a relationship between the presence of respiratory symptoms and positive skin tests, particularly to danders. This suggests that the increasing practice of keeping domestic animals in families and at schools may result in an increase in respiratory symptoms due to allergy to danders.

During the course of five years, the proportion of children with positive skin tests showed a two- to threefold increase with an increased intensity of the response. This con-

firms the common finding that antibodies to allergens are to a large extent produced at primary and secondary school age.

Radiography was not found to be very useful in differentiating between children with and without respiratory symptoms. This finding is in accordance with that reported by Simon et al. (45). These investigators observed marked radiological changes only in children with severe or moderately severe asthma which continued to cause symptoms.

7.2. PREVALENCE

The prevalence rates listed in Tables 8, 9*a*, 9*b*, 9*c*, 10*a* and 10*b* are based on the number of children of population A which took part in the study for a period of five years. The reasons for which children did not take part or no longer participated in the study are stated in section 4.3. These reasons did not include asthma, bronchitis or other respiratory conditions. In Table 20, the prevalence of symptoms in the children of population A in 1968 and 1972 is compared with that of the children who dropped out. The prevalence of symptoms during the last year in which these drop-outs took part in the study was that used in the table. The prevalence rates show only slight differences; the prevalence of symptoms in those who dropped out is slightly lower than it is in those who took part for five years. These may therefore be regarded as a random sample of the children of the two birth cohorts living in Hoogvliet and IJsselmonde on October 1, 1967. The symptom-positive groups include those children who satisfy the criteria of CNSRD applying to adults.

As has been mentioned earlier, the effect of the symptoms cough for three or more months a year and two consecutive months a year on pulmonary function is comparable with that of cough for three or more consecutive months a year. Tables 21 and 22 show the prevalence rates for the children of the symptom-positive groups when the criterion of cough (C II) is altered from cough for three or more conse-

cutive months a year to cough for three or more months a year and/or two or more consecutive months a year. When these criteria are applied, prevalence increases by 3–4 percent in the two youngest groups and by 1–2 percent in the older groups. The percentage of children included in one of the symptom-positive groups for two or more consecutive years also shows a slight increase. The general prevalence pattern, however, remains almost unchanged. This would not be the case if the symptom "wheezing" were to be added as a criterion for classification within one of the symptom-positive groups. The proportion of children which would then be included in these groups is much higher, as is shown in Table 23. However, as stated on p. 18, "wheezing" may be regarded as a secondary symptom.

Although approximately 50 percent of the children of the oldest birth cohort turned out to be smokers at 14–16 years of age (Table 24), this does not affect the prevalence of symptoms in this cohort.

As stated previously, the increase in the prevalence of the symptom-positive groups, which occurred in the 12th–13th year of life as compared with the previous year, is caused by an increase in the symptom dyspnoea on exertion. This increase is unlikely to have been due to smoking.

The prevalence rates determined in the present study are comparable only in part with those recorded by Knol (29), as this author took the recent and previous histories into account in calculating prevalence. The prevalence rates reported in the present paper were based only on recent histories. Comparison with the prevalence rates reported by others is not possible because of the differences in criteria as has been mentioned in the introduction.

7.3. RELATIONSHIP BETWEEN RESPIRATORY SYMPTOMS AND EXOGENOUS FACTORS

7.3.1. Air pollution

There was no difference between the prevalence of respiratory symptoms in Hoogvliet and that in IJsselmonde. The anticipation, based on the results of measurements carried out in 1967 and previous years, that pollution by sulphur dioxide and smoke during the period of investigation would be much more marked in Hoogvliet than in IJsselmonde was not realized. Therefore, it was not possible to determine whether the prevalence of prolonged cough or dyspnoea increases with the degree of air pollution.

Studies in other areas of the Netherlands (Westland, Zuid-Beveland) have shown that this is actually the case where cough is concerned (6, 27). The problem of short-lived respiratory symptoms resulting from air pollution could not be examined in the present study.

7.3.2. Social and demographic factors

It has been reported several times in the literature that respiratory symptoms become increasingly common in children as they live in worse social conditions (10, 11, 17).

In order to determine the effect of air pollution under the best possible conditions of life, the study was done in districts marked by an adequate social level. Section 6.6. shows that slight social differences do not affect the prevalence of respiratory symptoms. Providing optimum housing is essential to effective treatment and prevention of chronic or recurrent respiratory symptoms.

7.3.3. Smoking

Children of the youngest birth cohort may be assumed to be non-smokers. The proportion of children of the oldest birth cohort who stated in an inquiry that they regularly smoked cigarettes was 24 percent in 1970, 51 percent in 1971 and 57 percent in 1972 (Table 24). As these statements were anonymous, the existence of a possible correlation between symptoms and cigarette smoking could not be examined. However, our results showed that the overall-prevalence of respiratory symptoms did not increase at the ages at which regular smoking starts. In accordance with the findings reported by Colley (14, 15) and unlike those reported by a number of other investigators, there was no evidence

that so-called passive smoking due to parental smoking had any appreciable effect on the appearance of respiratory symptoms in school-children. For a review of the literature on smoking and its effects on health in children, the reader is referred to Bewley et al. (4) and to Appendix V.

7.3.4. *Respiratory symptoms in parents*

There is a definite relationship between respiratory symptoms in parents and those in children. This finding is also in accordance with that reported by Colley (14, 15).

Smoking may be taken to cause an increase in respiratory symptoms in the parents and thus indirectly to affect the symptoms in the children. However, repeated studies on the subject as well as a study of the relative contributions of endogenous (genetic) factors (2, 5, 38) and exogenous factors are still required.

7.4. LONGITUDINAL TREND

The present study was designed to get an impression of the longitudinal trend of symptoms of CNSRD in each child on the basis of particular features. As was apparent from section 6.2.2, the symptoms will merely cause a slight average decrease in pulmonary function and the mean pulmonary function values usually are within two standard errors of the normal mean values. This means that the pulmonary function parameters adopted ($FEV_{1.0}$, $FEV_{1.0}$%) are less useful in estimating the trend in each individual than are the symptoms. This also holds true for the histamine threshold, skin allergy and X-rays.

Very few children were found to have shown a particular symptom for more than two years or to have belonged to one of the symptom-positive groups for more than two years. Table 25, however, shows that the respiratory symptoms in a large proportion of these children were less marked in other years. It would therefore appear to be justifiable in principle to regard schoolchildren in whom symptoms of prolonged cough or dyspnoea occur, even if

only incidentally, as individuals with "chronic" respiratory disease (which does not imply that this actually is the case with all of these children).

In this context, "chronic" only means that the symptoms recur but does not say anything of the frequency and severity of these symptoms. Although it could be of importance to determine these for reasons of prognosis (42), this cannot be done with the questionnaire used.

In the population studied, therefore, only qualitative measurements of respiratory symptoms were carried out. Only studies in populations followed from childhood up to adult life will be able to show whether any prognostic value can be attached to these measurements. Studies by Colley (12, 13) suggest that this is the case. As the period for which the populations were followed was only five years, it is not possible to form an opinion on this subject as a result of the present study.

On the other hand, efforts were made to gain an impression of the extent to which the previous history is an important factor in the symptom pattern during the period of investigation. For this purpose, the number of times that questions on the previous history were answered in the affirmative or in the negative was studied with regard to the symptoms "cough for three or more months a year", "cough for three or more consecutive months a year", "cough for two consecutive months a year", "cough for one consecutive month a year", "dyspnoea on exertion", "asthmatic attacks" and "rhinitis".

For each of the above symptoms and for eight questions referring to the previous history, the percentage of children answering in the affirmative was divided by that answering in the negative. This quotient represents the relative risk that a symptom which occurred in the previous history will recur in the recent history (7). All of this is included in Table 26 which shows that respiratory symptoms at a young age involve an obvious risk of recurring later in life.

As stated in the introduction, a justifiable opinion on the future course of a "chronic" respiratory condition in the individual child usually cannot be formed. From the point of

view of prevention, it would therefore seem advisable to consider symptoms such as prolonged cough or dyspnoea (regardless of their severity or frequency) in all schoolchildren as potential "risks" of CNSRD in adult life.

This implies that adverse exogenous factors should be avoided wherever possible and that symptoms should be treated by the best possible method. This means in practice:

(1) Prompt treatment of bronchial obstruction and respiratory infections, if necessary daily drug treatment and physical therapy.

(2) Prevention of bronchial obstruction and respiratory infection by avoiding exogenous factors known to be liable to cause symptoms in a particular individual.

(3) Improving housing and adverse social and psychological conditions.

(4) Preventing the children from smoking by personal counseling and health education.

(5) Vocational guidance, counseling on habits of life, etc., if required.

(6) Measles and influenza vaccination.

Controlled screening of children with "chronic" respiratory disease at primary and secondary schools by the school health officer would be advisable. This can be done by using a simple questionnaire. Experience elsewhere (27) showed that a brief questionnaire completed by the parents at home will usually serve the purpose.

Attending physicians (general practitioners as well as specialists) should be more keenly aware of the need for "preventive treatment" than they are today.

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APPENDIX I. QUESTIONNAIRE

Text Questionnaire

[a] Questions concern the past 2 years.
[b] Questions concern the past year.

	1968[a] Question number	1969–1972[b] Question number		1968[a] Question number	1969–1972[b] Question number
I. Cough			Did your child usually bring up phlegm in winter during the day or at night?	8	—
Did your child *usually* cough when getting up in the winter? (Usually: that is about 5 days a week.) (Exclude clearing throat or a single cough.)	1	1	Did your child bring up phlegm like this on most days, for as much as three months a year?	9	13
Did your child *usually* cough during the day or at night in winter?	2	2	At what age did your child start bringing up phlegm?	10	—
Did your child *usually* cough when getting up in the summer? (Usually: that is about 5 days a week.) (Exclude clearing throat or a single cough.)	—	3	Did your child in the previous two years have a period of an increase in cough and phlegm lasting for three weeks or more? (Use this formulation for children who usually cough and bring up phlegm.) If "yes" has been answered to this question:	11	—
Did your child *usually* cough during the day or at night in summer?	—	4	Did your child have such a period more than once?	12	—
Did your child cough *like this* on most days for as much as three or more month a year?	3	5			
Did your child cough *like this* on most days in winter, for as much as three or more consecutive months?	4	6	**III. Dyspnoea**		
Did your child cough *like this* on most days in winter, for as much as two consecutive months?	—	7	Put "1" in square if the child is disabled from walking by any condition other than lung disease.	13	14
Did your child cough *like this* on most days in winter for as much as one consecutive month?	—	8	Has your child ever been troubled by shortness of breath when cycling against the wind or running?	14	—
Did your child cough *like this* on most days in summer for as much as three or more consecutive months?	5	9	Has your child ever been troubled by shortness of breath when playing outdoors or walking up a staircase?	15	—
Did your child cough *like this* on most days in summer for as much as two consecutive months?	—	10	Has your child regularly been troubled by shortness of breath when playing outdoors or walking up a staircase?	16	—
Did your child cough *like this* on most days in summer for as much as one consecutive month?	—	11	Did your child have to stop regularly because of breathlessness and sit down when playing outdoors or walking up a staircase?	17	—
At what age did your child start coughing?	6	—	Has your child ever been troubled by shortness of breath when playing outdoors or walking up a staircase in winter?	—	15
Did your child ever have periods of cough for as much as three consecutive months in the previous years?	—	12	Has your child regularly been troubled by shortness of breath when playing outdoors or walking up a staircase in winter?	—	16
II. Phlegm					
Did your child usually bring up phlegm when getting up in winter?	7	—			

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Text Questionnaire (continued)

	1968[a] Question number	1969–1972[b] Question number
Did your child have to stop regularly because of breathlessness and sit down when playing outdoors or walking up a staircase in winter?	—	17
Has your child ever been troubled by shortness of breath when playing outdoors or walking up a staircase in summer?	—	18
Has your child regularly been troubled by shortness of breath when playing outdoors or walking up a staircase in summer?	—	19
Did your child have to stop regularly because of breathlessness and sit down when playing outdoors or walking up a staircase in summer?	—	20
Has your child ever been troubled by shortness of breath when playing outdoors or walking up a staircase in the previous years?	—	21
At what age did you notice for the first time the breathlessness of your child? (Accept "around this age".)	18	22
IV. Wheezing		
Did your child ever wheeze in the previous years?	19	—
Did your child ever wheeze during the past winter?	—	23
Did your child wheeze most days or nights in winter?	—	24
Did your child wheeze two times or more? (If "no" proceed to "V Asthmatic attacks", if "yes" proceed to the next question.)	20	—
Does your child wheeze most days or nights?	21	—
Did your child ever wheeze during the past summer?	—	25
Did your child wheeze most days or nights in summer?	—	26
Does your child wheeze all days or nights?	22	—
At what age did your child start wheezing?	23	—
V. Asthmatic attacks		
When resting, did your child ever have attacks of shortness of breath with wheezing (asthmatic attacks)?	24	—

	1968[a] Question number	1969–1972[b] Question number
When resting, did your child ever have attacks of shortness of breath with wheezing (asthmatic attacks) in winter?	—	27
When resting, did your child ever have attacks of shortness of breath with wheezing (asthmatic attacks) in winter in the previous years?	—	28
When resting, did your child ever have attacks of shortness of breath with wheezing (asthmatic attacks) in summer?	—	29
When resting, did your child ever have attacks of shortness of breath with wheezing (asthmatic attacks) in summer in the previous years? (If "no" proceed to "VI Nasal catarrh", if "yes" proceed to the next question.)	—	30
At what age did your child first have these attacks? (Accept "around this age".)	25	31
At what age did your child last have these attacks? (Accept "around this age".)	26	32
Is your child ever short of breath when resting?	27	—
VI. Nasal catarrh		
Did your child ever have a stuffy or a running nose?	—	33
Has your child usually been troubled by a stuffy nose or nasal catarrh?	29	—
Have these troubles been present on most days for as much as three or more consecutive months? a. in winter; b. in summer.	30	—
Has your child usually been troubled by a stuffy nose or nasal catarrh in the past winter?	—	34
Have these troubles been present on most days for as much as three or more consecutive months in winter?	—	35
Have these troubles been present on most days for as much as two consecutive months in winter?	—	36
Have these troubles been present on most days for as much as one month in winter?	—	37

Text Questionnaire (continued)

	1968[a] Question number	1969-1972[b] Question number		1968[a] Question number	1969-1972[b] Question number
Has your child usually been troubled by a stuffy nose or nasal catarrh in the past summer?	—	38	Have these troubles been present on most days for as much as one consecutive month in summer?	—	41
Have these troubles been present on most days for as much as three or more consecutive months in summer?	—	39	**VII. *Previous diseases***		
			Did your child ever have:	36	47
			Eczema?	36a	47a
Have these troubles been present on most days for as much as two consecutive months in summer?	—	40	The tonsils removed?	36e	47e
			Attacks of bronchitis or asthma?	36h	47h
			Periods of cough?	36i	47i
			Pneumonia?	36j	47j

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APPENDIX II. OBSERVER'S ERRORS

Several investigations have been carried out on the comparability of medical histories taken by various interviewers in an epidemiological study.

Cochrane and Chapman (1) differentiate between two potential types of error:

1. Inter-observer's errors: errors appearing as differences between the results obtained by investigators.

2. Intra-observer's errors: errors appearing when the results obtained by a particular interviewer are different when he repeats his study in the same individuals. This is due, among other things, to the fact that one interview may affect the answers given during another interview. Kinsey et al. (4) therefore recommend an interval of at least eight months between two interviews of the same subject.

Cochrane and Chapman (1) had various interviewers question a large number of miners on respiratory and other symptoms. A standardized questionnaire was not used in this case, although efforts were made to standardize the technique of interviewing wherever possible in the survey.

The results obtained by the interviewers showed marked differences as regards the symptoms cough, pain in the chest and dyspepsia. The answers to those questions which had previously been discussed and standardized by the interviewers among themselves (such as the question on exertional dyspnoea) showed less disagreement between the interviewers.

It is concluded by these authors that careful standardization of questions is a condition essential to obtaining comparable results.

Schilling et al. (6) studied medical history-taking and physical examination by two physicians who took turns in examining one half of a group of individuals at a four-month interval. They observed significant differences between the results obtained by the two investigators concerning the results of physical examination and those of history-taking. They believe the differences in the results of history-taking to have been due to the following factors:

1. A difference in the answers given to the same question by the interviewee.

2. The fact that the answer given was influenced by the interviewer.

3. Different interpretations of the same answer by different interviewers. (Standardization of answers does not ensure standardization of interpretation.)

Fairbairn, Wood and Fletcher (2) believe that the initial stages of chronic bronchitis can only be recognized by the medical history. If the epidemiology of chronic bronchitis is to be studied, the results of various investigations will have to be comparable. Where medical histories are concerned, comparison will be possible only when a standardized questionnaire is used. The authors carried out a survey in which a standardized questionnaire was employed by six different investigators: three physicians and three health visitors distributed at random over the interviewees. This made it possible to compare the physicians and health visitors as groups and as individual investigators. The interviews were recorded on tapes and played back later. The subjects interviewed were postmen and women sorters in London. They were unselected; their ages ranged from forty to fifty-nine.

Two interviews were conducted at an interval of at least four weeks. Care was taken to prevent the interviewee from being interviewed twice by the same person. In four questions, there were significant differences among the physicians on the one hand and the health visitors on the other.

In thirteen questions, there were significant individual differences among the results. Of these, four were due to differences among the

physicians; the other nine were due to differences among the health visitors.

The differences concern only *affirmative* answers.

Among others, these differences were due to the following causes:

(1) The same interviewees gave different answers to questions put in the same way by the two interviewers.

(2) The health visitors as a group more often rated vague answers as positive than did the physicians as a group.

(3) When a question was answered in the negative, some interviewers asked questions which they should not have asked according to the protocol.

(4) The results suggested that questions which were not put clearly were occasionally answered in the affirmative, even though they had not been properly understood.

(5) The speed with which the interview was conducted influenced the number of affirmative answers, particularly the answers to questions on the previous history of disease.

(6) In a number of cases, the question stipulated was asked in a different (suggestive) manner.

(This mistake was made particularly when the question was formulated in such a way that it was not easy to ask it in a natural manner).

(7) In three per cent of the cases, incorrect recording by the interviewer was the cause of the differences.

Causes of 149 differences in results in nine questions

Cause	Number	Percentage
Interviewer	93	62
Interviewee	32	21
Question	24	16
	149	100

The differences were caused by the interviewers in 62 per cent of the cases; this was mainly due to the fact that they did not stick to the literal wording of the questions. As a re-

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sult, an unduly large number of affirmative answers was obtained.

The difference between the two most experienced interviewers was as large as that between any other pair of interviewers.

Several investigators (3) (5) (7) are engaged in developing other methods of medical history-taking. The most recent procedure is a questionnaire controlled by a computer.

Questions appear on a screen; the interviewee selects one of four numbered answers: - yes, no, I don't know, I don't understand. He presses the corresponding button and, depending on his answer, the computer will either proceed to the following general question or cause a more detailed question on the same subject or some further explanation to appear on the screen. This basic technique is currently being developed to a further extent; among others, by improving understanding and co-operation on the part of the interviewees. In the Mayo Clinic, for instance, the questions are illustrated by drawings. These methods may improve the possibilities of standardization. The answers are immediately ready for processing in the computer. Drawbacks are the considerable expense, the fact that only a limited number of individuals can ben "interviewed" at the same time as well as the fact that errors cannot be traced to their source later on.

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APPENDIX III. HISTAMINE THRESHOLD AND INITIAL
PULMONARY FUNCTION

INTRODUCTION

Many stimuli having a local action (pharma-cological, physical, allergic stimuli) may cause swelling of the mucosa, hypersecretion and contraction of the smooth muscle tissues in the bronchi. The degree of "reactivity" will vary from one individual to another. The histamine threshold or acetylcholine threshold (the lowest concentration of histamine or acetylcholine resulting in a decrease of $\geqslant 15$ per cent of the vital capacity, or the one-second forced expiratory volume, or other measures of bronchial obstruction) are often adopted as parameters of this reactivity (3).

De Vries (4) pointed out that initial pulmonary function (measured as the one-second forced expiratory volume) and the histamine threshold are not independent of one another. He posed the question whether the histamine threshold may be regarded as a correct parameter of reactivity or whether it merely is an indirect measure of bronchial obstruction. He concluded that, rather than the histamine threshold as such, an index derived from it, the so-called reactivity score might provide a superior parameter of bronchial reactivity.

Cade and Pain (1) observed no relationship between the acetylcholine threshold and initial pulmonary function in asthmatic patients free of symptoms. During a symptom-free interval, the acetylcholine threshold was found to be constant over a period of a few weeks.

METHODS

The relationship between the histamine threshold (3) and the pulmonary function values one-second forced expiratory volume (FEV_1), peak expiratory flow (PEF) and vital capacity (VC) was studied in children with chronic nonspecific respiratory disease who attended the outpatient department for respiratory diseases of the Sophia Children's Hospital and in children who took part in the population survey. Follow-up studies were done in these children to determine whether any trend of the histamine threshold values in a particular child is reflected in a similar trend of the pulmonary
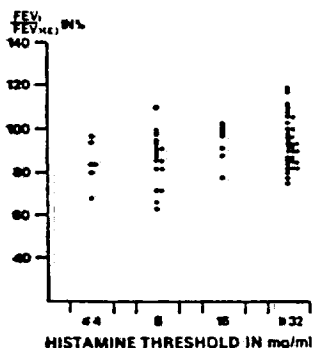
Fig. 1. Relationship between $FEV_1/FEV_{1(E)}$ and histamine threshold.
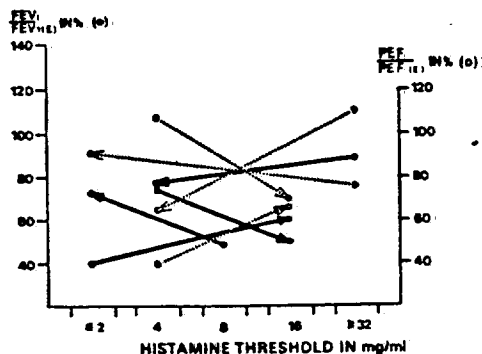
Fig. 2. Various relationships between pulmonary function and histamine threshold.

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Table 1. *Correlation between histamine threshold and initial pulmonary function in children with chronic nonspecific respiratory disease*

Histamine threshold (mg/ml)	$FEV_1/FEV_{1(E)}$[a]		$VC/VC_{(E)}$[a]		$PEF/PEF_{(E)}$[a]	
	Mean value	Number examined	Mean value	Number examined	Mean value	Number examined
< 2	0.77	12	0.97	12	0.93	13
4	0.85	18	1.03	18	0.97	11
8	0.90	7	0.99	7	0.96	8
16	1.02	2	1.12	2	1.06	2
32	0.93	11	0.96	11	1.18	18

[a] (E) = height-adjusted mean value according to Polgar (2).

function values during the successive tests performed in that child. This was accomplished as follows. A score also used in Kendall's rank correlation test was calculated for each child per height-adjusted pulmonary function. For the relationship between the histamine threshold and $FEV_1/FEV_{1(E)}$, for instance, the following procedure was adopted:

Initially, those children in whom both the histamine threshold and the FEV_1 had been determined in more than one study were selected. All tests performed in these children were compared in pairs. When two tests are performed, one paired comparison is possible ($1 \rightarrow 2$, $1 \rightarrow 3$, $2 \rightarrow 3$); when four tests are performed, six paired comparisons are possible, etc. A partial score which may assume the values -1, 0 or $+1$, is added to each paired comparison. This partial score is calculated as follows:

Histamine threshold higher in second test than in first test, $FEV_1/FEV_{1(E)}$ being also higher: $+1$.

Histamine threshold higher in second test than in first test but $FEV_1/FEV_{1(E)}$ lower: than in first but $FEV_1/FEV_{1(E)}$ lower: -1.

Histamine threshold lower in second test than in first test but $FEV_1/FEV_{1(E)}$ higher: -1.

[1] $FEV_1/FEV_{1(E)}$ means: one-second forced expiratory volume divided by the height-adjusted mean one-second forced expiratory volume.
$PEF/PEF_{(E)}$ and $VC/VC_{(E)}$ have a similar meaning. The height-adjusted mean values are according to Polgar (2).

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Histamine threshold lower in second test than in first test, $FEV_{1.0}/FEV_{1.0}$ exp. also lower: $+1$.

Histamine threshold and/or $FEV_{1.0}/FEV_{1.0}$ exp. equal in the two tests: 0.

For this purpose, the histamine thresholds were classified into the following groups: ≤ 4, 8, 16 and ≥ 32 mg/ml. Two values of $FEV_{1.0}/FEV_{1.0}$ exp. were regarded as being different as soon as they were unequal. Although a difference of two values, ranging from $+5$ per cent to -5 per cent, does not necessarily mean that there is an actual difference but may be due to variability in the measuring technique, every difference was regarded as an actual difference in calculating the partial score. A longitudinal relationship, if any, will thus be more likely to be detected than it will when values differing from each other by less than 5 per cent are considered to be equal.

The total score of a child for the relationship

Table 2. *Correlation between histamine threshold and initial pulmonary function in a random population of 11-year-old boys and girls*

Histamine threshold (mg/ml)	$FEV_1/FEV_{1(E)}$[a] Mean value	$VC/VC_{(E)}$ Mean value	Number examined
< 4	0.85	0.96	6
8	0.86	0.90	16
16	0.94	0.96	7
32	0.93	0.95	32

[a] See Table 1.

between the histamine threshold and $FEV_1/$ $FEV_{1(E)}$ exp. then will be the sum of the partial scores of all paired comparisons. When two tests have been performed in a child, the total score may therefore assume the values $+1$, 0 or -1. When three tests have been performed, the total score may assume all the values from -3 up to and including $+3$, and it may assume all the values from -6 up to and including $+6$ in the event of four tests.

The same method was used in calculating the total scores of each child for the relationship between the histamine threshold and the $VC/$ $VC_{(E)}$ exp. and, if determined, for the relationship between the histamine threshold and the $PEF/PEF_{(E)}$.

RESULTS

(1) Transversal study

Tables 1 and 2 show the mean initial pulmonary function values for each histamine threshold. There is a linear relationship between the intial value of $FEV_1/FEV_{1(E)}$ or $PEF/PEF_{(E)}$ and the 2 logarithm of the histamine threshold, which is significant at the 5 per cent level test. This means that, starting from the null hypothesis that there is no relationship between the initial pulmonary function value and the histamine threshold, the likelihood that there is a linear trend such as that present in this case or that there is an even more marked linear trend will be smaller than or equal to 5 per cent. Therefore, the null hypothesis at a 5 per cent level has to be rejected. There is no such relationship between the VC and the histamine threshold.

(2) Longitudinal study

The total scores per pulmonary function parameter for a number of the children listed in Tables 1 and 2 as well as for a number of other children are shown in Tables 3 and 4. In a large number of cases, this total score is found to be nil. As is shown by Tables 5 and 6, this is usually due to the fact that the value of the histamine threshold is identical in all studies. Therefore, it could not be concluded from these

Table 3. *Scores of histamine thresholds and initial pulmonary functions at repeated examinations, children with CNSRD, number of children*

Score	Number of examinations		
	2	3	4
$FEV_1/FEV_{1(E)}$ [a]			
+6			
+5			
+4			
+3		1	1
+2		7	
+1	4	1	
0	13	19	
−1	9		
−2		2	
−3			
−4			
−5			
−6			
Total number of children	26	30	10
$VC/VC_{(E)}$ [a]			
+6			
+5			
+4			
+3			2
+2		8	1
+1	6	2	
0	14	17	7
−1	6	1	
−2		2	
−3			
−4			
−5			
−6			
Total number of children	26	30	10
$PEF/PEF_{(E)}$ [a]			
+6			
+5			
+4			
+3			
+2			
+1	14		
0	17		1
−1	16	1	
−2		1	
−3		1	
−4			
−5			
−6			
Total number of children	47	3	1

[a] See Table 1.

findings that, as a rule, the trend of the histamine thresholds is identical with a similar trend of pulmonary function values during

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Table 4. Scores of histamine thresholds and initial pulmonary functions at repeated examinations in a random population of boys and girls, 11–13 years of age, number of children

	Number of examinations		
Score	2	3	4
FEV₁/FEV₁(E)*			
+6			
+5			
+4			2
+3		1	5
+2		2	
+1	4		2
0	15	6	17
-1	4	1	
-2			
-3			2
-4			
-5			
-6			
Total number of children	23	10	28
VC/VC(E)*			
+6			
+5			
+4			
+3		1	4
+2		1	1
+1	5		3
0	15	8	18
-1	3		
-2			2
-3			
-4			
-5			
-6			
Total number of children	23	10	28
PEF/PEF(E)*			
+6			
+5			
+4		1	
+3		1	
+2		4	1
+1	5	2	
0	22	10	3
-1	5		1
-2		2	
-3			
-4			
-5			
-6			
Total number of children	32	19	5

* See Table 1.

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successive studies. This similarity was therefore examined with regard to the VC and FEV₁ in twenty and with regard to the PEF in twenty-two children. The results are listed in Table 7. These show that there is usually an adequate relationship between the trend of pulmonary function values and that of the histamine threshold values in the children studied.

COMMENT AND CONCLUSIONS

Though significant, the relationship between the initial values of the FEV₁/FEV₁(E) or PEF/PEF(E) exp. and the initial value of the histamine threshold is rather weak. This is also apparent from Figure 1 in which the initial values of the FEV₁/FEV₁(E) of a number of children who took part in the population survey have been plotted against their histamine thresholds. When the histamine threshold of a child is given, the FEV₁/FEV₁(E) cannot be even approximately predicted, nor can the histamine threshold of a child be

Table 5. Number of children examined twice and scoring 0, CNSRD

	Histamine threshold	Number
FEV₁/FEV₁(E)*		
Higher	Equal	8
Equal	Higher	
Equal	Equal	
Equal	Lower	
Lower	Equal	5
Total		13
VC/VC(E)*		
Higher	Equal	6
Equal	Higher	
Equal	Equal	1
Equal	Lower	1
Lower	Equal	6
Total		14
PEF/PEF(E)*		
Higher	Equal	10
Equal	Higher	
Equal	Equal	
Equal	Lower	
Lower	Equal	7
Total		17

* See Table 1.

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Table 6. *Number of children examined twice and scoring 0, selected at random*

	Histamine threshold	Number
FEV₁/FEV₁₍ₑ₎ [a]		
Higher	Equal	9
Equal	Higher	
Equal	Equal	1
Equal	Lower	
Lower	Equal	5
Total number		15
VC/VC₍ₑ₎ [a]		
Higher	Equal	8
Equal	Higher	
Equal	Equal	
Equal	Lower	
Lower	Equal	7
Total number		15
PEF/PEF₍ₑ₎ [a]		
Higher	Equal	10
Equal	Higher	
Equal	Equal	1
Equal	Lower	1
Lower	Equal	10
Total number		22

[a] See Table 1.

predicted when its $FEV_1/FEV_{1(E)}$ is known. The weakness of the relationship between the two quantities is also illustrated in the value for the coefficient of correlation of the $FEV_1/FEV_{1(E)}$ and 2 log of the histamine threshold, viz., 0.32.

As is shown in a number of children in Figure 2, a child showing a histamine threshold which is twice or four times as high in a follow-up study as it was in the initial test may yet show a much lower $FEV_1/FEV_{1(E)}$ or $PEF/PEF_{(E)}$, and vice versa in the second study. Table 7 shows that the trend of the $FEV_1/FEV_{1(E)}$ was the reverse of that of the histamine threshold in eight out of twenty children and that the trend of the $PEF/PEF_{(E)}$ was the reverse of the histamine threshold in six out of twenty-two children. It would therefore appear justifiable to conclude that the histamine threshold value and the pulmonary function values measured in this study were mainly determined by different factors.

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Table 7. *Pulmonary function at first and second histamine threshold, children with CNSRD (number of children)*

	First histamine threshold compared with second histamine threshold								
	VC/VC₍ₑ₎ [a]			FEV₁/FEV₁₍ₑ₎ [a]			PF/PF₍ₑ₎ [a]		
	Higher	Equal	Lower	Higher	Equal	Lower	Higher	Equal	Lower
First histamine threshold at least 2 steps lower than second threshold	6	0	3	4	0	5	4	0	8
First histamine threshold at least 2 steps higher than second threshold	8	1	2	7	0	4	7	1	2

[a] See Table 1.

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APPENDIX IV. AIR POLLUTION AND RESPIRATORY DISEASE

1. INTRODUCTION

There is no consensus regarding the importance of air pollution as a factor in the patho- genesis and course of respiratory disease. A large number of investigators believe, however, that air pollution has an adverse effect.

Pollution of the outdoor air may be caused by:

(1) *Reducing substances.* These mainly consist of sulphur compounds (sulphur dioxide, sul- phuric acid and sulphates), smoke and soot. Reducing substances are believed to be the most injurious to health.

(2) *Oxidizing substances.* These mainly con- sist of hydrocarbons, nitrous oxide and photo- chemical reaction products (ozone, aldehydes, ketones). Sunlight is required as a catalyst to produce these last-named substances. Oxidizing substances cause irritation of the mucosae of the eyes, nose and throat in susceptible indi- viduals. Although they may induce symptoms in subject with chronic respiratory disease, they apparently affect morbidity and mortality to a lesser extent than do reducing substances.

The air inhaled will be polluted, for instance, by indoor factors under particular conditions of work, when the discharge of products of combustion in houses is inadequate and as a result of smoking. Studies on the effects of short- and long-term exposure to polluted air on the respiratory system is numerous.

The present authors confine themselves to the most important studies on the subject. For a comprehensive review of the literature, readers are referred to the Air Pollution Abstracts (published by the National Air Pollution Control Association) and Environmental Health published by Excerpta Medica.

The following abbreviations have been em- ployed in the present paper:

PEF = peak (expiratory) flow
(F)VC = (forced) vital capacity
$FEV_{1.0}$ = one second forced expiratory volume
$FEV_{0.75}$ = identical with $FEV_{1.0}$ but 0.75 sec instead of one second.

2. STUDIES ON THE SHORT-TERM EFFECTS OF AIR POLLUTION

2.1. In children

Anderson and Larsen (1) studied nonattendance and the incidence of respiratory disease in children in the first form of the primary schools in three localities in British Columbia for a period of six months. Two of these localities were adjoining residential areas situated under the smoke of an industry; the third was a non- industrial residential area which was chosen because its climate was comparable with that of the other two. Studies were made to deter- mine whether the incidence of respiratory disease was higher in the two first-named areas. There was no significant difference in school absences among the three residential areas but respiratory infections and other forms of disease were more common and more prolonged in the children living in the polluted areas than they were in those living in the nonpolluted area; peak flow values were also significantly lower in the children living in the polluted areas.

Lunn et al. (20) studied 819 Sheffield infant school children living in districts in which the degree of air pollution (sulphur dioxide and smoke) differed widely. Infections of the upper as well as those of the lower respiratory tract were found to be more common in the more polluted districts. Socioeconomic factors such as social class, size of the family and housing were of minor importance. Pulmonary function parameters ($FEV_{0.75}$ and FVC) were not

affected by socioeconomic factors or air pollution, except in the most severely polluted area, where these pulmonary function values showed a significant decrease. Four years later, follow-up studies were done in 558 of these children at the age of 9 (21). Respiratory symptoms were less common than they had been four years previously, and there were no longer any differences among the various residential districts. These improvements were accompanied by a decrease in the overall air pollution level in Sheffield and a reduction in the differences in air pollution among the districts themselves.

Girsh et al. (11) studied the relationship between weather conditions and air pollution on the one hand and peaks in the incidence of attacks of asthma on the other by recording the number of patients with attacks of asthma attending the out-patient department of a Philadelphia children's hospital daily for two years. This number was three times as high on days marked by a measurable increase in air pollution (sulphur dioxide, nitrous oxide, carbon monoxide and soot). Attacks of asthma were four times as common on days marked by a high atmospheric pressure as they were on days marked by a low atmospheric pressure. During the period of investigation, high atmospheric pressure accompanied by increased air pollution was present on 117 days. The incidence of attacks of asthma on these days showed a ninefold increase compared with that on days on which the air was cleaner and less stagnant.

Ferris (9) studied school absences in approximately 700 first and second graders of seven primary schools in Berlin (New Hampshire) over a period of eighteen months. The schools were situated in areas in which air pollution (sulphur dioxide and smoke) differed markedly. Differences in school absence were not observed. However, the PEF, FVC and FEV$_{1.0}$ values measured during the second period of investigation were significantly higher than were those in children of schools in the nonpolluted districts. This was not adequately accounted for by differences in social class. The author believes that the differences in pulmonary

function values may have been due to differences in air pollution (see also 24).

Chiaramonte et al. (5) studied 429 children attending the emergency room in the children's ward of Long Island College Hospital, New York for three weeks, which included a few days with a marked increase in air pollution (sulphur dioxide). Eighty-three of these children showed respiratory conditions; the majority were hospitalized during or just after the period of air pollution. The number of children admitted for obstructive respiratory disease was larger during or just after the air pollution peak than it was during the other periods. The differences were statistically significant.

McMillan et al. (22) studied pulmonary function in third graders of two primary schools in two towns marked by different degrees of air pollution (sulphur dioxide, nitrous oxide, soot). Pulmonary function values (PEF) were measured by a peak-flow meter twice monthly for eleven months, invariably at 1 p.m., the time at which the concentration of oxidant air pollution was believed to be highest. The studies were done to examine whether:

(1) Sudden changes in oxidant air pollution are associated with changes in PEF. There was no evidence to suggest that this was so. There was a constant difference between the mean PEF in the children of the two schools but a decrease in mean PEF was not associated with an increase in air pollution in either of the two groups.

(2) Prolonged exposure to air pollution is associated with a permanent decrease in PEF. The mean PEF in the children attending the school in the most severely polluted area was found to be constantly higher than it was in those attending the school in the less severely polluted area.

(3) Symptoms of infection of the upper respiratory tract are associated with prolonged exposure to air pollution. The incidence of infection of the upper respiratory tract was almost three times as high in children attending the school in the less severely polluted area.

2.2. In adults

Lawther et al. (17) studied the relationship between respiratory symptoms and air pollution in cases of chronic bronchitis in London by having the patients record their symptoms every day. The sulphur dioxide and smoke concentrations were measured at seven points in Inner London; the patients all lived or worked in Greater London. In 1959–1960, a positive relationship between air pollution and an increase in symptoms during the early part of the winter was found (November). This relationship was no longer present at the end of the winter (February). This survey, which was carried out for the first time during the winter of 1954 to 1955, is now being repeated in London every five years.

For a period of six months, *Shy* et al. (24) studied the incidence of acute respiratory disease in families having a child attending an elementary school as a second grader. The studies were done in four districts of Greater Chattanooga: one in which air pollution by nitrous oxide was very severe, another which was polluted by particles floating high in the air and two "clean" areas. More cases of respiratory disease were constantly observed in the two first-named areas, particularly during the outbreak of influenza A2. This difference in the incidence of acute respiratory disease in the various areas could not be accounted for by the family constellation or social class.

As part of a triennial follow-up study of the populations of Vlagtwedde and Vlaardingen, *Van der Lende* et al. (18) studied the VC and $FEV_{1.0}$ in Vlaardingen during a short period of increased air pollution in October 1969 and compared the findings with those during a period of low air pollution. They observed a transient decrease in VC and $FEV_{1.0}$ during this period. These authors conclude that spirometry probably is a more sensitive method than medical history-taking in measuring the effects of air pollution peaks.

3. STUDIES ON THE LONG-TERM EFFECTS OF AIR POLLUTION

3.1. In children

Douglas and *Waller* (8) studied 3 866 children from birth in 1946 up to the age of 15 (1961). These children had been living in 2 689 different residential areas since their birth. Each of these residential areas was classified into one of four categories according to the degree of air pollution (sulphur dioxide and smoke). The results were simple and constant in character: conditions of the upper respiratory tract were not affected by the degree of air pollution but the incidence and severity of diseases of the lower respiratory tract were greater in those areas in which air pollution was more severe. This correlation was present at every age. There was no difference between the sexes or between different social classes.

Biersteker (3) observed no difference between the height-adjusted mean peak flow rate in 500 Rotterdam school children living in a central district in which air pollution (sulphur dioxide and smoke) was relatively severe and that in 500 school children living in a nonpolluted suburban district.

Holland et al. (13) studied 10 971 children in four Kent districts showing various degrees of air pollution (sulphur dioxide and smoke). The mean PEF in children living in the most severely polluted area was lower than that in children living in the less severely polluted areas. This was independent of social class, size of the family and previous respiratory disease (which also was a factor in itself). It is concluded from these findings that air pollution probably results in changes in the respiratory tract during childhood. These changes possibly continue to be present throughout life and may contribute to the subsequent development in chronic respiratory disease.

Shy et al. (24), who studied second graders in four districts of Greater Chattanooga marked by different degrees of air pollution (nitrous oxide), found the $FEV_{0.75}$ to be lower in children in the district showing the highest degree of

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pollution than it was in children living in the "clean" control areas.

Colley and Reid (7) studied over 10 000 6–10-year-old children in various districts of England and Wales which showed different degrees of air pollution (sulphur dioxide and smoke). Previous histories of chronic cough, disease of the upper respiratory tract and "bronchitis" were more common in the lower than they were in the higher social classes. The prevalence of chronic cough and disease of the upper respiratory tract increased with the local degree of air pollution only in the children of social classes IV and V (unskilled and semi-skilled workers).

Sultz et al. (26) studied 617 children hospitalized for asthma over a period of five years and found air pollution to increase the incidence and severity of attacks of asthma.

Zapletal et al. (27) studied the effect of air pollution (sulphur dioxide) on various parameters of pulmonary function in 111 children showing no respiratory symptoms and who had been living in a highly polluted area for at least five years. The FVC, $FEV_{0.75}$ and $FEV_{1.0}$ were within normal limits in all children. Six children with a low normal FEV showed a reduced expiratory flow when the vital capacity was low. This is indicative of obstruction of the respiratory tract. As these children had had no recent or previous respiratory disease in so far as this could be verified, the authors believe that the obstruction of the bronchi may have been due to air pollution.

Shy et al. (25) studied pulmonary function ($FEV_{0.75}$) in children attending primary schools in areas marked by high and low degrees of air pollution in Cincinatti, Chattanooga and New York (suspended particles, sulphur dioxide and nitrous oxide). There was a constant relationship between diminished pulmonary function in 5–13-year-old children and exposure to air pollution. In Cincinnatti, pulmonary function improved during periods of slight air pollution but failed to increase to the level of those living in areas constantly marked by only a small degree of pollution. The findings in 9–13-year-old children in New York showed that exposure to high degrees of air pollution in early childhood for periods ranging from five to ten years may result in a prolonged decrease in $FEV_{0.75}$.

In Chattanooga, the effect of exposure to an increased concentration of nitrous oxide for a period varying from two to three years was not measurable to any appreciable extent.

Grosse et al. (12) studied the relationship between air pollution and pulmonary function in 1 930 school children in two towns in the German Democratic Republic showing different degrees of air pollution (sulphur dioxide and smoke) in 1970. Children living in the most highly polluted area usually showed a decrease in VC and FEV values.

As part of the Euro 3114 project of the WHO in Copenhagen, Kerrebijn and Biersteker (15) did a study on children in the Westland area of the Netherlands. Here, there is a high degree of exposure to sulphur dioxide as a result of the fact that a large number of hothouses are heated with sulphurous oil. The results were compared with those obtained in children living in an area in which exposure to sulphur dioxide is low. About 2 400 children of the fourth and fifth forms of the primary school in the two areas, participated in the study which took place in the spring and early summer of 1973. The findings showed that the symptoms wheezing and rhinnorrhoea and the appearance of bronchitis or pneumonia were commoner in the polluted areas. The mean $FEV_{0.75}$ and FVC were also found to be lower in the polluted districts.

3.2. In adults

Oshima et al. (23) studied the effect of air pollution (sulphur dioxide) on the respiratory tracts of Japanese subjects in an area marked by a relatively low degree of pollution (Niigata) and compared this effect with that in a similar population group in an area showing a high degree of pollution (Tokyo, Yokohama). Pulmonary function tests were performed (FVC and $FEV_{1.0}$); 2 765 subjects took part in this study. The inhabitants of Tokyo and Yoko-

hama produced larger quantities of sputum and more frequently showed chronic cough and irritation of the throat. Of these, cigarette smokers and subjects having previous histories of allergy showed the largest number of symptoms. The mean FVC was lower in the inhabitants of this area than it was in the inhabitants of Niigata, and this was particularly so in those who had been living in Tokyo and Yokohama for a considerable period.

Holland and Reid (14) studied the incidence of respiratory symptoms, sputum production and pulmonary function ($FEV_{1.0}$ and PEF) in the drivers of mail and delivery vans in the city of London and the towns of Gloucester, Peterborough and Norwich. Particularly from the age of fifty, symptoms were more common and more severe in the Londoners; they produced larger average quantities of sputum and showed lower mean pulmonary function values. There was a definite relationship between personal smoking habits and the incidence and severity of the symptoms in each population studied. However, the difference between urban and rural smoking habits failed to account for the higher incidence of respiratory symptoms in London. It is concluded by the authors that this higher incidence of symptoms was due mainly to the difference in air pollution (sulphur dioxide) between central London and the three country towns.

Biersteker (2) examined 1 000 Rotterdam municipal officers for symptoms of bronchitis. He observed a number of subjects showing bronchitis; the number increased with age. Those affected with bronchitis smoked a significantly larger number of cigarettes than did those free of bronchitis. The average period for which they had been living in Rotterdam (adopted as a measure of exposure to air pollution) did not differ in those with and those without symptoms.

Lambert and Reid (16) studied the incidence of respiratory disease in 9 975 men and women in the 35–69 year range using a postal questionnaire. Chronic respiratory symptoms were found to be more common in smokers and to increase with age. Men showed symptoms more frequently than women (both smokers and non-smokers). The differences between urban and rural areas were not solely accounted for by differences in smoking habits. Air pollution (sulphur dioxide and smoke), however, apparently did not affect nonsmokers to an appreciable extent. There seems to be an interaction between smoking and air pollution, resulting in an increased prevalence of respiratory disease in smokers living in highly polluted areas. This becomes particularly apparent with increasing age.

Cohen et al. (6) studied the incidence of cough, sputum production and a number of pulmonary function parameters in two comparable groups of nonsmoking adults permanently exposed to identical mean but different peak degrees of air pollution (sulphur dioxide, nitrates, sulphates). There were no significant differences between the two groups.

Ferris et al. (10) reported the results of a follow-up study of adults in Berlin, New Hampshire, in 1961 and 1967. Even when the effects of ageing and changes in smoking habits were taken into account, cases of respiratory disease were found to be less common in 1967. The fact that the average results of pulmonary function studies (FVC and $FEV_{1.0}$) in 1967 were superior to those obtained in 1961 was in accordance with this finding. Air pollution (sulphur dioxide and soot) was less marked in 1967 than it was in 1961. The authors believe that this accounts for the decrease in the incidence of respiratory disease and the improvement in pulmonary function values.

Since 1965, Van der Lende et al. (19) have been doing comparative follow-up studies on the incidence of chronic nonspecific respiratory disease among the inhabitants of a rural area (Vlagtwedde) and those of an air-polluted area (Vlaardingen). The pollutants are sulphur dioxide, soot, nitrous oxide and hydrocarbons. The studies also include "micropollution" in the two environments (smoking habits, occupational activities, type of heating, etc.). The prevalence of chronic cough and expectoration

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SUMMARY: Thirty-five children known to have had respiratory syncytial virus bronchiolitis in infancy were examined at the age of 8 and their respiratory function tested. The results were compared with those in 35 controls matched for age, sex, and social class.

Although 18 of the children who had had bronchiolitis in infancy had experienced subsequent episodes of wheezing, these were neither severe nor frequent in most cases and had apparently ceased by the age of 8. Nevertheless, the mean exercise bronchial lability of the children who had had bronchiolitis was significantly higher than that of the control children and the mean peak expiratory flow rate at rest significantly lower. Atopy, assessed by family and personal history alone, did not seem to be related to either bronchiolitis or wheezing episodes after bronchiolitis. The parents of the children who had had bronchiolitis smoked significantly more cigarettes during the infant's first year of life than those of the control children.

The results suggest that bronchiolitis and childhood asthma are not closely related. Bronchial hyperreactivity might be inherited independently of atopy, but environmental factors seem the most likely link between severe respiratory infection in infancy and chronic or recurrent respiratory illness in adult life.

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the severity of the clinical symptoms could not be adequately explained by valvular regurgitation, of which there was little evidence on examination of the heart. Blood cultures usually remained sterile, presumably because of inappropriate antibiotic treatment or the limited infectiveness of the organisms present, or both.

A striking feature in three patients (cases 1, 2, and 4) was the acute, severe, and rapidly resolving but recurrent episodes of pulmonary oedema. Possibly these were caused by sudden blocking of the orifice by vegetation—this was indeed shown echocardiographically in one patient (case 4). Other patients (cases 3 and 5 and those reported by Reeve et al[1] and Matula et al[2]) had more progressive pulmonary oedema, suggesting increasing mitral stenosis. In our experience both types of pulmonary oedema are uncommon in patients with isolated mitral valve regurgitation during bacterial endocarditis.

Those of our patients who did not have mitral valve replacement (cases 2, 4, and 5) and the patient of Reeve and his colleagues[1] had a sudden cardiac arrest. Mitral valve vegetations cause obstruction just as catastrophic as an atrial tumour or a ball thrombus, and hence once the doctor suspects mitral valve obstruction he should confirm the diagnosis promptly and ensure that the patient is rapidly operated on.

Accurate diagnosis is vital. Right heart catheterisation showed a raised pulmonary wedge pressure without a striking V wave, but was nevertheless of little value in assessing the severity of the haemodynamic disturbance: pressures may be very high because of rheumatic valve disease (case 4) or only moderately increased because the obstruction is intermittent. Echo-cardiography is the only method of detecting valvular vegetations directly: bulky vegetations such as occurred in these patients are unlikely to be missed. The technique has only a limited sensitivity, however, in mitral valve endocarditis.[3][4] Linear echoes behind the mitral valve should not be confused with atrial myxoma[5]; fungal,[3] marantic,[6] or granulomatous[7] obstruction; or thrombus.

Hence whenever pulmonary oedema occurs in a patient with fever, haemodynamic oedema resulting from bacterial endo-carditis should be suspected routinely even if the findings on cardiac auscultation are normal. A viral origin is unlikely if fever continues for more than a week. Cardiac catheterisation may not confirm the diagnosis and echocardiography should be used. When this gives abnormal echoes behind the mitral valve in a patient with the typical history and other features, emergency surgery should be carried out because of the risk of sudden death.

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Study of 8-year-old children with a history of respiratory syncytial virus bronchiolitis in infancy

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Summary and conclusions

Thirty-five children known to have had respiratory syncytial virus bronchiolitis in infancy were examined at the age of 8 and their respiratory function tested. The results were compared with those in 35 controls matched for age, sex, and social class.

Although 18 of the children who had had bronchiolitis in infancy had experienced subsequent episodes of wheezing, these were neither severe nor frequent in most cases and had apparently ceased by the age of 8. Nevertheless, the mean exercise bronchial lability of the children who had had bronchiolitis was significantly higher than that of the control children and the mean peak expiratory flow rate at rest significantly lower. Atopy, assessed by family and personal history alone, did not seem to be related to either bronchiolitis or wheezing episodes after bronchiolitis. The parents of the children who had had bronchiolitis smoked significantly more cigarettes during the infant's first year of life than those of the control children.

The results suggest that bronchiolitis and childhood asthma are not closely related. Bronchial hyperreactivity might be inherited independently of atopy, but environmental factors seem the most likely link between severe respiratory infection in infancy and chronic or recurrent respiratory illness in adult life.

Introduction

Does lower respiratory tract infection in infancy increase the risk of recurrent or chronic respiratory disease in later life? Difficult though this question is the answer may provide important new incentives for preventing and managing severe respiratory illness at all ages, and in recent years relevant evidence has been accumulating. A history of lower respiratory tract illness in early childhood has been shown to be associated with an increased incidence of respiratory symptoms and impaired ventilatory function in later childhood and early adult life.[1-4] Many children with a history of recurrent wheezing become symptom free but respond abnormally to exercise

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tests.[*] In all these studies, however, the definition of the early illness has been uncertain, depending largely on parental diagnosis or on retrospective clinical judgment.

Respiratory syncytial (RS) virus bronchiolitis is the commonest severe lower respiratory tract infection in infancy. Its characteristic clinical picture and viral cause provide an opportunity to define a more homogeneous group of children for follow-up studies. Rooney and Williams[*] followed such a group, and their finding that 35 out of 62 children known to have had RS virus bronchiolitis in infancy developed subsequent wheezing episodes has often been quoted. Their study was not controlled, however, and at follow-up the children's ages ranged from 2 to 7 years.

We therefore identified a group of children who had had RS virus bronchiolitis in infancy and studied them eight years later. The assessment included tests of respiratory function as well as history and examination. Information was gathered about manifestations of atopy and smoking habits in the child's family, as both may be relevant to the development of recurrent or chronic respiratory illness. All the results were compared with those from a control group of children matched by age, sex, and social class and known not to have been admitted with bronchiolitis in infancy. The Newcastle Area Health Authority Ethical Committee agreed to the study.

Method

The records of all infants from whom RS virus was isolated in the winter epidemic of 1967-8 were examined. Fifty-six infants (29 girls and 27 boys) had one or more signs of bronchiolitis recorded and were selected. One of the 56 children has since died of aspiration pneumonia after ingesting polystyrene fragments, and two had emigrated. No attempt was made to contact a child with multiple congenital abnormalities and another with severe mental retardation. Of the remainder, four lived 100 miles or more away, two could not be traced, and five refused to attend for follow-up.

We were able to match 35 children closely with 35 controls and these were included in the study. At the time of their admission in infancy with RS virus bronchiolitis wheezing had been recorded in 33, chest recession in 30, crepitations in 29, and clinically detectable overinflation in nine. Radiological appearances of the chest had been reported as being normal in 11 and showing overinflation in 15, subsegmental collapse or consolidation in 11, peribronchial thickening in six, and segmental consolidation in one. Clinically this child with segmental consolidation had had recession, wheezing, and bilateral crepitations.

The 35 children were reviewed with one or both parents and details of subsequent respiratory illnesses were obtained. Parents were asked whether the child or any first-degree relatives had a history of wheezing (they were asked: "Has a whistling sound ever come from the chest?" and the sound was demonstrated by a forced expiration); eczema (a red, flaking, itchy rash); allergic rhinitis (nasal discharge, sneezing, or irritation of the eyes at certain times of the year or with specific allergens); urticaria (pale, itchy, raised bumps on the skin); or rashes in response to food or drugs. Family smoking habits during the child's first year of life and currently were recorded. The weight and height of each child were noted and the upper and lower respiratory tract examined clinically. Resting values of forced expiratory volume in 0·75 second ($FEV_{0.75}$) and vital capacity (VC) were measured using a Vitalograph spirometer. The peak expiratory flow rate (PEFR) was measured with a Wright's peak flow meter, and the value was taken as the best of three readings after the child had become accustomed to the procedure and was giving consistent values. The child then ran for six minutes round a quadrangle or up and down a corridor and the pulse was counted. PEFR readings were obtained during a pause for a few seconds three minutes after starting to run, and at one, three, five, 10, and 15 minutes after completing the run. From these readings the maximum percentage rise and fall of PEFR were determined. Exercise-induced bronchial lability was expressed as the sum of the percentage maximum rise and fall of PEFR.[*] One child had a PEFR at rest of less than 50% of the expected mean normal and was therefore not exercised.

Control children were identified by giving lists containing the sex, age, and social class of the index children to the headteachers of four Tyneside schools. The headteachers were asked to select children of the same sex and age to within two months and to attempt to match the social class using father's occupation as a guide. The parents then were approached by letter. Thirty-five children were investigated by the same methods as the index children. None of the control children had been admitted to hospital during the first year of life with respiratory illness. All the interviews and tests were carried out by the same person.

Results were compared using Student's t test for matched pairs, χ^2 tests, and exact probability tests for qualitative data.

Results

COMPARABILITY OF THE TWO GROUPS

The only significant difference between the groups was in the mean number and age of siblings, both of which were greater in the bronchiolitis group (table I).

CLINICAL HISTORY AND EXAMINATION

Eighteen of the children who had had bronchiolitis gave a history of wheezing on one or more occasions since their bronchiolitis compared with only one of the control group ($P < 0.0005$). The wheezing episodes experienced subsequently by the children who had had bronchiolitis were, however, neither severe nor frequent enough to have resulted in hospital outpatient or inpatient referral. The episodes were often absent for long periods, and 10 of the 18 children had experienced no wheezing at all in the two years before interview.

There was a slightly higher incidence of a history of upper respiratory tract infections and croup among the children who had had bronchiolitis, but this difference did not reach statistical significance. Routine physical examination of the upper and lower respiratory tract showed no significant differences between the two groups.

TESTS OF RESPIRATORY FUNCTION

Table II shows the mean values for $FEV_{0.75}$, VC, PEFR at rest, and $FEV_{0.75}$ as a percentage of VC. The PEFR values were significantly lower in the children with a history of bronchiolitis ($P < 0.02$). No significant difference was demonstrable between the groups for $FEV_{0.75}$ or VC values, but for the $FEV_{0.75}$ expressed as a percentage of the VC the mean value in the bronchiolitis group was lower by 4·1% which was statistically significant ($P < 0.05$). Immediately after exercise the mean pulse rate was 182 ± 12.1 beats/min in the bronchiolitis group and 184 ± 19.5 beats/min in the controls, suggesting that exertion was comparable in the two groups

TABLE I—*Comparability of the two groups of children studied. Results are means ± SD*

Group	No of children	Sex (F M)	Mean birth weight (kg)	Mean age at interview (years)	Mean current weight (kg)	Mean current height (cm)	Mean No of siblings	Mean age of siblings (years)	Social class distribution		
									I and II	III	IV, V, and other*
Bronchiolitis	35	18 17	3·22 ± 0·49	8·32 ± 0·28	26·56 ± 4·00	127·9 ± 6·39	2·1 ± 1·45	10·9 ± 5·13	2	19	14
Control	35	18 17	3·32 ± 0·46	8·40 ± 0·33	26·20 ± 3·95	126·4 ± 5·25	1·3 ± 0·86	8·5 ± 4·17	3	23	9
Mean difference			−0·10	−0·08	+0·36	+1·5	+0·8	+2·4	χ^2 (DF = 1) = 1·619; P > 0·2		
Standard error of difference within pairs			0·122	0·042	1·013	1·490	0·315	0·943			
P value			> 0·4	> 0·05	> 0·7	> 0·3	< 0·02	< 0·02			

Unemployed, disabled, etc.
Difference between means.
Significant at 0·05 level.

TABLE II—*Results of tests of respiratory function made at rest*

Group	No of matched pairs	Mean value	Mean difference	Standard error of difference	P
FEV₀·₇₅(l)					
Bronchiolitis	35	1·59	−0·05	0·067	>0·4
Control		1·64			
VC (l)					
Bronchiolitis	34	1·95	+0·06	0·084	>0·4
Control		1·89			
PEFR (l/min)					
Bronchiolitis	35	237·3	−27·8	11·358	<0·02
Control		265·1			
FEV₀·₇₅/VC × 100					
Bronchiolitis	34	83·2	−4·1	1·827	<0·05
Control		87·3			

Mean (±SD) PEFR change in response to exercise for bronchiolitis and control groups. Comparisons were made in matched subjects.
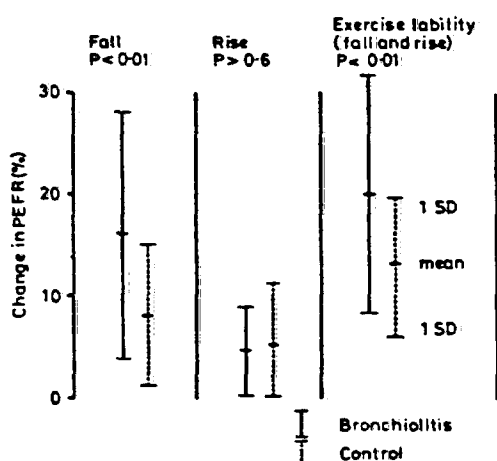
(P>0·5). The figure shows the mean indices of bronchial lability. The mean differences in values for percentage fall and for exercise lability were significant (P<0·01). Exercise testing precipitated symptoms in two children: one child in the bronchiolitis group with an exercise lability of 70% developed severe wheezing, and one control child with an exercise lability of 35%, whose parents had never noticed wheezing previously, had a transient episode of coughing and wheezing after the test.

ATOPY

The prevalence of clinical features of atopy in the children and their first-degree relatives was similar in the two groups.

PARENTAL SMOKING HABITS

During the infant's first year of life 71% of the mothers of children who had had bronchiolitis had smoked compared with 49% of control mothers, a difference that just failed to reach statistical significance (χ^2 with 1 DF=3·81; P>0·05). More fathers of children in the bronchiolitis group had smoked (77%) than control fathers (60%) but this difference was not significant (P>0·1).

Together the parents of children who had had bronchiolitis had smoked on average 29·1 cigarettes/day during the first year of the infant's life, compared with 19·6 smoked by the control parents. This gave a mean difference of 9·5 cigarettes/day with a standard error of 4·125, which was significant (P<0·05).

At the time of the study the parents whose children had had bronchiolitis smoked on average 29·2 cigarettes/day and the control parents 21·1, a mean difference of 8·1 with a standard error of 4·947. This was not statistically significant (P>0·1).

COMPARISONS WITHIN BRONCHIOLITIS GROUP

Further analyses were made after dividing the bronchiolitis group into those with a subsequent history of wheezing (18 children), and those without (17 children). No significant differences in sex distribution, social class, age at interview, birth weight, or current weight and height emerged when these subgroups were compared. Retrospective analysis of details of the original admission for bronchiolitis with respect to age, weight, use of antibiotics, length of hospital stay, physical signs, and radiological findings, showed no differences. There were also no differences in the prevalence of atopy or in parental smoking habits.

Table III gives results of lung function tests at rest and during exercise for the wheezing group, the non-wheezing group, and the controls. The PEFR values at rest, the fall in PEFR during exercise, and overall exercise lability showed a consistent trend, the wheezing children performing worse than the non-wheezing children, who in turn performed worse than the controls. There was no such trend for the rise in PEFR during exercise.

Discussion

Eighteen of the children with a history of RS virus bronchiolitis suffered subsequent wheezing, but it was rarely severe, was often absent for long periods, and in most cases had apparently ceased by the age of 8. We therefore suggest that the clinical prognosis for a baby with RS virus bronchiolitis is good, at least at the age of 8, and disagree with Rooney and Williams's conclusion that there may be a strong association between bronchiolitis and unequivocal asthma.[1] There does, however, seem to be an association with the syndrome described by Williams and McNicol[2] of mild infrequent wheezing episodes that resolve by the age of 8. Leeder et al[3] have recently shown that there is a relation between a history of pneumonia or bronchitis in infancy and subsequent wheezing and that this relation is stronger for wheezing not regarded by parents as "asthmatic."

Exercise lability studies at this age have not been reported in a group of this size. The test was performed with ease on most of the children, but a few needed extra encouragement and a

TABLE III—*Results of lung function tests in bronchiolitis group subdivided into those with and those without a history of subsequent wheeze and compared with their matched controls*

	PEFR at rest (l/min)		Maximum rise in PEFR (%)		Maximum fall in PEFR (%)		Exercise lability (%)	
	No	Mean ± SD	No	Mean ± SD	No	Mean ± SD	No	Mean ± SD
Bronchiolitis—further wheezing (A)	18	226·4±49·5	17*	5·6±4·9	17*	17·1±15·9	17*	22·7±15·0
Controls (CA)	18	269·4±49·6	17	3·9±4·4	17	7·4±5·7	17	11·3±4·7
Bronchiolitis—no further wheezing (B)	17	248·8±35·4	17	2·8±3·5	17	14·3±6·9	17	17·1±6·0
Controls (CB)	17	260·6±37·4	17	5·6±7·4	17	8·4±8·1	17	14·0±8·3
Significance:								
A v B		>0·1		>0·05		>0·5		>0·1
A v CA		0·02		>0·3		<0·05		<0·02
B v CB		>0·4		>0·2		<0·05		>0·2

*Values in one subject were not measured.

few were so eager to oblige that they were inclined to blow hurriedly into the peak flow meter without inhaling fully unless closely watched. The mean exercise lability of the children who had had bronchiolitis in infancy was significantly higher than that of the control children and the mean PEFR at rest significantly lower. Whether these findings have implications for the development of chronic respiratory illness in adult life will be known only after many years of further observation.

Rooney and Williams' thought that they had shown an association between family atopy and the development of wheezing episodes after bronchiolitis, but their data were incomplete, and some of their younger children may have developed wheezing later in childhood after a latent period. In our study there was no apparent link between atopy and either bronchiolitis or subsequent wheezing. Clinical questioning, however, is an unreliable measure of atopy and we plan to investigate the two groups of children further by skin tests and IgE estimations.

Our results suggest that cigarette smoking by the parents during the infant's first year of life may be associated with an increased risk of RS virus bronchiolitis for their baby. To establish this a study of smoking and non-smoking parents would be necessary. Similar associations between parental smoking and lower respiratory tract infection in infancy have been found by other investigators.[10-12]

There are three possible ways in which respiratory disease in infancy may be linked with that in later life: there may be a causal link between the two, a genetic predisposition to both, or common environmental factors. Of the three, a causal link, although it cannot be excluded, is perhaps unlikely in view of the small degree of respiratory disability we found in the 8-year-old children who had had bronchiolitis in infancy and the long symptom-free period that many of them had experienced. We have so far been unable to show that atopy constitutes a genetic link. McNicol and Williams have already speculated that bronchial hyperreactivity may be inherited independently of atopy,[13] and the results of our exercise tests are not inconsistent with this suggestion.

Environmental factors such as overcrowded housing, family

size, air pollution, and cigarette smoking are increasingly recognised as influencing the prevalence of respiratory illness in children as well as adults.[3 9 14 15] Parental smoking was more common and family size larger in our bronchiolitis group, and the persistence of these factors may explain, at least in part, why many children went on to have further episodes of wheezing with impaired ventilatory function. Matching groups of children by father's occupation conceals wide variations in the way children are cared for,[16] and a search for more subtle differences in the home environment between children with and without respiratory disease may disclose new opportunities for prevention.

We are grateful to the four headmasters for their help in identifying the control children and providing facilities for testing them and to the Medical Research Council for their support.

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Antinuclear antibodies in patients receiving non-practolol beta-blockers

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Summary and conclusions

Antinuclear antibodies (ANA) were found in 54 (7·0%) out of 767 treated hypertensive patients compared with 59 (2·4%) out of 2470 healthy controls. Inclusion of a non-practolol beta-blocker in the treatment regimen did not significantly affect the incidence of ANA. ANA was found in significantly more patients being treated with methyldopa (13·0%) than patients receiving other hypotensive agents (3·8%). Non-practolol beta-blockers in combination with methyldopa did not increase the incidence of ANA further.

Introduction

Recognition that patients taking the beta-adrenoceptor-blocking drug practolol may develop serious oculomucocutaneous reactions[1] has raised concern about the toxicity of related drugs. There is little evidence that non-practolol beta-blockers induce similar reactions, despite the awareness of practitioners and government agencies of side effects. Practolol toxicity was not recognised until cumulative experience with the drug totalled one million patient-years,[2] and some patients developed symptoms only after many months of treatment or even after the

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Fergusson, D.M., Horwood, L.J., Shannon, F.T. "Parental smoking and respiratory illness in infancy" <u>Archives of Disease in Childhood</u> 55(5): 358-361, 1980.

SUMMARY: The relationship between parental smoking and respiratory illness in a birth cohort of 1180 one-year-old children was examined. Maternal smoking was associated with an increased incidence of lower respiratory illness but there was no statistically significant association between paternal smoking and lower respiratory illness. While children of mothers who smoked suffered more lower respiratory illnesses, their overall risk of respiratory infection was similar to that for children of nonsmoking mothers. The association between maternal smoking and infantile lower respiratory illness persisted when the child's social background, perinatal history, and postnatal diet were taken into account. The findings favour the view that prolonged exposure to cigarette smoke predisposes infants to develop lower respiratory symptoms when they contract a respiratory infection.

(5)

Parental smoking and respiratory illness in infancy

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SUMMARY The relationship between parental smoking and respiratory illness in a birth cohort of 1180 one-year-old children was examined. Maternal smoking was associated with an increased incidence of lower respiratory illness but there was no statistically significant association between paternal smoking and lower respiratory illness. While children of mothers who smoked suffered more lower respiratory illnesses, their overall risk of respiratory infection was similar to that for children of nonsmoking mothers. The association between maternal smoking and infantile lower respiratory illness persisted when the child's social background, perinatal history, and postnatal care were taken into account. It was concluded that smoking during and after pregnancy predisposes infants to develop lower respiratory symptoms when they contract a respiratory infection.

A number of studies has shown that parental smoking is related to an increased risk of bronchitis and pneumonia among children under one year[1-2] and to an increased risk of morning cough and breathlessness among schoolchildren.[3-6] The association between parental smoking and lower respiratory illness in children has been shown to persist when factors—such as, family size, birthweight, social class, the child's smoking habits—are taken into account.[1-36] This paper examines the effects of parental smoking on the risk and nature of respiratory illness during the last 8 months of the first year of life in a birth cohort of 1180 infants.

Method

The data were collected during the third stage of the Christchurch Child Development Study.[7] In this project a cohort of infants was studied at birth, at 4 months, and one year. At birth, the child's mother was interviewed, using a structured schedule, to find out the background to the pregnancy and the antenatal history. When the child was 4 months old, the mother was again interviewed, using a structured schedule, to find out about the child's health and development since birth, the diet, and the social and economic background of the family. At one year a similar interview was administered. At each inter-

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view the mother signed a consent form indicating her willingness to participate in the research.

The initial cohort comprised 1262 children and one year later 1180 were still in the study. This represented 94% of the initial cohort and 97% of the children who were still alive and resident in New Zealand. The following measures were used in the analysis.

Measures of respiratory illness. To measure respiratory illness, both that involving medical consultation and that treated at home, two measures of respiratory illness were constructed.

Medical consultation

At 4 months and again at one year the child's mother was asked to give details of the child's history of medical consultation. While maternal reports of medical consultation are unlikely to be completely accurate, Colley[5] found there was good agreement between such reports and medical records. From the maternal reports of medical consultation, a child was defined as having a *lower respiratory illness* if he had attended a medical practitioner or a hospital for bronchitis, bronchiolitis, or pneumonia. A child was defined as suffering an *upper respiratory illness* if he had attended a medical practitioner or hospital for respiratory illness other than bronchitis, bronchiolitis, or pneumonia.

Symptoms

To supplement the data on medical consultations each mother was asked whether the child had

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displayed any of a series of respiratory symptoms, irrespective of whether he had seen a doctor. From this questioning two measures were constructed. The first was whether the child had ever suffered a 'wheezy chest' and the second was whether he had ever suffered other respiratory symptoms such as cold, sore throat, sore ears, etc. Questioning on symptoms was only conducted at one year, so that complete medical data on the child were available only for the period from 4 months to one year. Because of this, the analysis is restricted to the last 8 months of the child's first year of life.

Parental smoking. Parents were classified as 'smoker' or 'nonsmoker'.

Perinatal history, social background, and diet measures. The following variables were used in the analysis for purposes of statistical control: birth-weight, gestational age, maternal age, maternal education, maternal race, number of children in the family, family living standards, and duration of breast feeding.

The joint effects of maternal and paternal smoking on the risk of lower respiratory illness were analysed using the logistic analysis of factorial designs described by Cox.[8] In this analysis maternal and paternal smoking were treated as two factors and the proportion of infants with lower respiratory illness was the dependent variable. This proportion was transformed using the logistic function and contrasts of the effects of maternal smoking, paternal smoking, and the maternal/paternal smoking interaction were examined.

Results

Tables 1 and 2 show the relationship between parental smoking and the risk of medical attendance for lower respiratory illness, and maternal reports of wheezy chest during the last 8 months of the first year of life.

Table 1   *Percentage of children with medical consultation for lower respiratory illness by parental smoking**

Father	Mother		
	Nonsmoker	Smoker	Overall
Nonsmoker†	6 (n = 588)	10 (n = 190)	7 (n = 778)
Smoker	6 (n = 192)	14 (n = 199)	10 (n = 391)
Overall	6 (n = 780)	12 (n = 389)	8 (n = 1169)

*Excludes 11 children for whom data were missing for either smoking or respiratory illness.
†Includes 88 families in which there was no father, or father figure.

Table 2   *Percentage of children with wheezy chest by parental smoking**

Father	Mother		
	Nonsmoker	Smoker	Overall
Nonsmoker†	29 (n = 588)	38 (n = 190)	31 (n = 778)
Smoker	30 (n = 192)	43 (n = 199)	36 (n = 391)
Overall	29 (n = 780)	40 (n = 389)	33 (n = 1169)

*Excludes 11 children for whom data were missing for either smoking or wheezy chest.
†Includes 88 families in which there was no father, or father figure.

there was no significant association between paternal smoking and lower respiratory illness ($P > 0.05$); there was no significant interaction between maternal smoking, paternal smoking, and the risk of lower respiratory illness ($P > 0.05$).

Table 3 shows the relationship between maternal smoking and the risk of all respiratory illness or symptoms. This risk is subdivided into upper respiratory illness or symptoms only (such as, nasal discharge, pharyngitis, otitis media, maternal reports of cold, sore throat) and lower respiratory illness or symptoms (such as, bronchitis, bronchiolitis, pneumonia, maternal reports of wheezy chest). Overall, the risk of respiratory illness was similar for the children of smokers and nonsmokers. However

Table 3   *Percentage of children with respiratory symptoms, upper respiratory symptoms only, lower respiratory symptoms, by maternal smoking*

Measure	Non-smoker (n = 786)	Smoker (n = 394)	Total (n = 1180)	P*
With at least one respiratory symptom	91	93	92	> 0.05
With upper respiratory symptoms only	63	52	60	< 0.001
With lower respiratory symptoms	29	40	33	< 0.001

*χ^2 test.

Table 4 . Risks of lower respiratory illness adjusted for perinatal factors, home background, and breast feeding

Measure	Adjustment				
	None	Perinatal history	Home background	Breast feeding	All factors
Medical consultations					
Nonsmoker (%)	6	6	6	6	6
Smoker (%)	12	12	12	12	12
Maternal reports of wheezy chest					
Nonsmoker (%)	29	28	29	29	29
Smoker (%)	40	41	40	40	40

symptoms about a lower risk of respiratory illness affecting only the upper respiratory tract.

To control for the effects of the child's perinatal history, home background, and postnatal diet, the binary multiple regression method described by Feldstein[9] was used. Table 4 shows for the two measures of lower respiratory illness: (1) The risk of lower respiratory illness for children of smoking and nonsmoking mothers, adjusted for the effects of birthweight and gestational age. (2) The risk of lower respiratory illness for children of smoking and nonsmoking mothers, adjusted for the effects of maternal age, education, ethnic status, family size, and family living standards. (3) The risk of lower respiratory illness for children of smoking and nonsmoking mothers, adjusted for the effects of duration of breast feeding. (4) The risk of lower respiratory illness for children of smoking and nonsmoking mothers, adjusted for the joint effects of the perinatal, home background, and diet measures.

It can be seen from Table 4 that the adjusted estimates of the risks of lower respiratory illness do not differ appreciably from the unadjusted risks. This indicates that the apparent association between maternal smoking and infantile lower respiratory illness cannot be explained by the confounding effect of dependence on perinatal history, home background, or postnatal diet.

Discussion

An association between parental smoking and infantile lower respiratory illness has been demonstrated.[1-8] The findings reported here extend knowledge of this association in a number of ways.

Perhaps the most interesting result is that, while maternal smoking was associated with an increased risk of infantile lower respiratory illness, there was no such association for paternal smoking. This difference has been overlooked in previous studies which have not considered the sex of the smoking parent. The obvious implication of the result is that duration of exposure to cigarette smoke (rather than the presence of a smoker in the house) is an important factor in the correlation.

Previous studies have considered the effects of parental smoking on lower respiratory illness only. The findings reported here show that there is a complicated relationship between parental smoking and all respiratory illness. Overall, the children of mothers who smoke do not have a greater risk of respiratory illness but they do have a greater risk of suffering illness which penetrates the lower respiratory tract. The mechanisms that underlie this effect are not well understood, but the obvious implication is that exposure to cigarette smoke facilitates the spread of infection to the lower respiratory tract.

In addition, previous research has examined the relationship between parental smoking and medical consultation for lower respiratory illness. Since medical consultations probably provide a biased sample of infant illness, there is the possibility that the apparent association between parental smoking and infant lower respiratory illness could have arisen from some bias in consulting practices. The results reported here suggest that maternal smoking is associated with an increased risk of lower respiratory illness whether or not these symptoms were treated by a medical practitioner.

Finally, the range of social and perinatal factors controlled in this study is greater than that considered in previous studies of the topic. On the basis of the findings reported here it may be concluded that the association between maternal smoking and infantile lower respiratory illness cannot be explained by the confounding effect of such factors as perinatal history, social background, or bottle feeding.

There now appears to be sufficient evidence to support the view that people in regular and prolonged contact with infants should not smoke, or if they must, they should not do so in the presence of infants.

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SUMMARY: The relationships between parental smoking and the rates of lower respiratory illness during the first three years of life were examined for a birth cohort of 1265 New Zealand children. Lower respiratory illness varied significantly with maternal smoking for the first year; there was equivocal evidence of a relationship between maternal smoking and lower respiratory illness in the second year; and by the third year the relationship had clearly disappeared. Paternal smoking had no significant effect on rates of lower respiratory illness at any time. Application of logistic regression showed that for the first year rates of lower respiratory illness were approximately linearly related to maternal smoking: increases of five cigarettes a day resulted in an increase of 2.5 to 3.5 incidents of lower respiratory illness per 100 children at risk. Statistical control for maternal age, education, family size, and family living standards showed that the relationship between maternal smoking and rates of lower respiratory illness was not significantly influenced by these factors.

Parental smoking and lower respiratory illness in the first three years of life

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SUMMARY   The relationships between parental smoking and the rates of lower respiratory illness during the first three years of life were examined for a birth cohort of 1265 New Zealand children. Lower respiratory illness varied significantly with maternal smoking for the first year; there was equivocal evidence of a relationship between maternal smoking and lower respiratory illness in the second year, and by the third year the relationship had clearly disappeared. Paternal smoking had no significant effect on rates of lower respiratory illness at any time. Application of logistic regression showed that for the first year rates of lower respiratory illness were approximately linearly related to maternal smoking: increases of five cigarettes a day resulted in an increase of 2·5 to 3·5 incidents of lower respiratory illness per 100 children at risk. Statistical control for maternal age, education, family size, and family living standards showed that the relationship between maternal smoking and rates of lower respiratory illness was not significantly influenced by these factors.

A number of studies have reported associations between parental smoking and lower respiratory illness in children. These reports have ranged from findings of increased rates of bronchitis and pneumonia in infants[1-4] to increased morning cough and breathlessness in children of school age.[1-8] Most authors have been cautious about imputing a causal relationship on the basis of the correlational evidence, but at least three sets of findings suggest that the relationships are causal rather than coincidental.

Firstly, the association between parental smoking and childhood respiratory illness has been remarkably resilient to attempts at statistical control. Various studies have shown that the correlation persists when such factors as family social conditions[1 2 4]; family composition[2 4]; perinatal history[2 4]; breast-feeding[4]; lower respiratory illness in the child's family[1 2]; and the child's smoking habits[8] have been taken into account.

Secondly, the correlation appears to be specific to lower respiratory illness and at least two studies[2 4] have reported that a similar association does not exist for upper respiratory illness.

Finally, a study by Fergusson, Horwood, and Shannon[4] indicated that the effects of smoking varied with the degree of contact between the smoking adult and the child: maternal smoking contributed significantly to lower respiratory illness in infants, but paternal smoking did not.

Despite the convergence of evidence suggesting a causal link between parental smoking and childhood lower respiratory illness, relatively little is known about the details of this association. In particular, information is absent or limited on the dose/response relationships which exist between parental smoking levels and rates of lower respiratory illness and the way in which the effects of parental smoking vary with the child's age.

In this paper we report on the results of a three-year prospective study of the effects of parental smoking on lower respiratory illness in children. The aims of the study were two-fold: to describe the way in which the effects of parental smoking on lower respiratory illness varied with the age of the child, and to provide estimates of the dose/response relationships between parental smoking levels and rates of lower respiratory illness.

Method

The data were collected during the first five stages of the Christchurch Child Development Study.[4 9] In this study a birth cohort of infants born live in the Christchurch (New Zealand) urban region during the period 15 April 1977 to 5 August 1977 has been studied at birth, four months, one, two, and three years. At each stage information was collected by structured interviews with the child's mother, supplemented by information from hospital records

and other sources. The topics examined by the interviews included the child's health, development, and family social and economic background.

Information on the medical history, including respiratory illness, of each child was collected in the following ways:

(1) During the periods birth to four months, one to two years, and two to three years each mother was provided with a diary in which to record her child's history of medical attendance. Compliance was good; 85% of mothers returned a diary record for the period from birth to four months and 60–65% for the periods between one and three years.

(2) At each interview the mother was asked to give details of her child's history of medical attendance. This information was obtained from the diary record where available or from maternal recall supplemented by telephone calls to the family doctor.

(3) The history of the child's hospital attendance was cross-checked against all available hospital records in Christchurch and by contacting hospitals outside the Canterbury region for relevant case information in other cases, subject to the signed consent of the mother. Comparison between maternal reports of hospital admission and hospital records revealed very good agreement between the two: only two mothers failed to report an admission for their child during the three-year period.

(4) Mothers were asked to provide data on the history of medical consultation, and were also questioned about the child's history of symptoms and illness which had not received medical treatment.

Using this information, it was possible to reconstruct the child's history of illness from birth to three years.

The following measures were used in the analysis:

(1) *Lower respiratory illness.* Two measures were constructed:

(a) Bronchitis/pneumonia—whether the child had attended a doctor or hospital for bronchitis, bronchiolitis or pneumonia during any of the periods birth to one year, one year to two years, and two to three years.

(b) Symptoms of lower respiratory illness—because measures of medically treated lower respiratory illness could have provided a biased estimate of morbidity, a second more general index was constructed. This was based on reports of medically treated bronchitis/pneumonia together with maternal reports of 'chesty cold' or 'wheezy chest' irrespective of whether medical treatment was sought. A child was defined as displaying symptoms of

lower respiratory illness if he had received medical attention for bronchitis/pneumonia or if his mother reported 'chesty colds' or 'wheeze'. (Incidents in which chest wheeze was ascribed to asthma were not included in the definition).

(2) *Parental smoking.* At one year, two years and three years information was obtained on both maternal and paternal daily cigarette consumption.

(3) *Control variables.* The following measures were used in the analysis for the purposes of statistical control: maternal age, education, family size, and an interviewer rating of family living standards. (These variables were selected on the basis of preliminary tabular and multiple regression analyses of a larger set of possible control factors including birthweight, gestational age, sex, maternal ethnic status, family composition, family income, and early infant diet. This analysis showed that only maternal age, education, family size, and living standards were related to both parental smoking habits and lower respiratory illness in childhood).

RESPONSE RATES AND MISSING DATA

Table 1 shows the response rates for each year of data collection. Response rates remained uniformly high over the three-year period. Of the initial cohort of 1265 infants, 1143 remained in the study at three years. This represented 90% of the initial cohort and 96% of the cohort who were still alive and resident in New Zealand. In a few cases (10 to 15 a year) data were missing on parental smoking or history of lower respiratory illness. All analyses are based on the sample available in each time-period who had complete data on all variables in the analysis. The sample sizes involved are given by the N's shown in Table 2. Comparisons of the social and demographic characteristics of the sample (that is, maternal age, education, ethnic status, family income, socioeconomic status) between interviews showed no significant differences in sample composition arising from sample losses.

Results

Table 2 shows the annual rates per 100 children of bronchitis/pneumonia and total lower respiratory

Table 1 *Response rates during the three-year study period*

Time	Number interviewed	% original sample (1265)	% of those alive and resident in New Zealand
One year	1180	93·3	96·8
Two years	1156	91·4	96·6
Three years	1143	90·4	96·4

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Table 2 Rates per 100 children of bronchitis/pneumonia and lower respiratory symptoms in the first three years of life by maternal and paternal smoking (number of children in brackets)

FIRST YEAR

Paternal smoking (cigs/day)	BRONCHITIS/PNEUMONIA			LOWER RESPIRATORY SYMPTOMS		
	Maternal smoking (cigs/day)			Maternal smoking (cigs/day)		
	0	1-10	11+	0	1-10	11+
0	7.0 (588)	12.8 (78)	13.4 (112)	37.6 (588)	47.4 (78)	50.9 (112)
1-10	4.6 (66)	14.0 (43)	11.1 (18)	37.9 (66)	53.5 (43)	33.3 (18)
11+	8.8 (125)	12.7 (55)	19.7 (81)	42.4 (125)	43.6 (55)	53.1 (81)

SECOND YEAR

Paternal smoking (cigs/day)	BRONCHITIS/PNEUMONIA			LOWER RESPIRATORY SYMPTOMS		
	Maternal smoking (cigs/day)			Maternal smoking (cigs/day)		
	0	1-10	11+	0	1-10	11+
0	9.1 (584)	20.7 (87)	13.2 (114)	43.8 (585)	54.0 (87)	50.9 (116)
1-10	7.9 (76)	3.3 (30)	12.0 (25)	44.7 (76)	51.6 (31)	36.0 (25)
11+	11.1 (108)	15.9 (44)	11.9 (67)	55.6 (108)	52.2 (46)	50.8 (67)

THIRD YEAR

Paternal smoking (cigs/day)	BRONCHITIS/PNEUMONIA			LOWER RESPIRATORY SYMPTOMS		
	Maternal smoking (cigs/day)			Maternal smoking (cigs/day)		
	0	1-10	11+	0	1-10	11+
0	8.9 (605)	5.5 (73)	12.1 (116)	37.4 (605)	39.7 (73)	45.3 (117)
1-10	11.8 (76)	8.7 (23)	8.0 (25)	41.6 (77)	21.7 (23)	36.0 (25)
11+	10.2 (108)	13.5 (37)	6.1 (65)	36.1 (108)	40.5 (37)	41.5 (65)

symptoms during the three-year study period. These rates are subdivided by maternal and paternal daily cigarette intake. A series of five log-linear models was fitted to the annual rate data to test for the presence of significant relationships between parental smoking behaviour and rates of lower respiratory illness. The method involved fitting a series of hierarchical models which differed from one another by one effect. From these models, tests of the contributions of maternal and paternal smoking behaviour to the rates of lower respiratory illness were derived from the differences between the values of the log-likelihood χ^2 statistic associated with each model. This analysis showed:

(1) For the first year, a model which assumed that the rates of childhood lower respiratory illness were independent of parental smoking did not fit the data. Further analysis showed that there was a significant tendency for rates of bronchitis/pneumonia (log $\chi^2 = 17.4$; df = 2;

$p < 0.001$) and of lower respiratory symptoms (log $\chi^2 = 12.4$; df = 2; $p < 0.01$) to vary with maternal smoking behaviour. Paternal smoking did not significantly contribute to the rates of lower respiratory illness either when considered alone or when maternal smoking behaviour was taken into account.

(2) For the second year, a model which assumed that the rates of lower respiratory illness were independent of maternal and paternal smoking behaviour was sufficient to fit the data for both bronchitis/pneumonia and total lower respiratory symptoms. However, for the bronchitis/pneumonia data it was found that a model which included maternal smoking as a factor related to lower respiratory illness resulted in a statistically significant improvement in the fit of the data over the model of the independence between the factors (log $\chi^2 = 8.3$; df = 2; $p < 0.02$). The results thus suggested an equivocal relationship between maternal smoking

Table 3 *Rates and differences in the rates per 100 children of bronchitis/pneumonia and total lower respiratory symptoms between children of non-smokers and smokers*

Year	BRONCHITIS/PNEUMONIA			LOWER RESPIRATORY SYMPTOMS		
	Mother Non-smoker	*Mother Smoker*	*Difference*	*Mother Non-smoker*	*Mother Smoker*	*Difference*
First	7·1	14·5	7·4	38·4	49·1	10·7
Second	9·1	14·2	5·1	44·9	50·8	5·9
Third	9·3	9·1	−0·2	37·6	40·6	3·0

and lower respiratory illness in the second year of life.

(3) For the third year, a model in which the rates of lower respiratory illness were assumed to be independent of maternal and paternal smoking was sufficient to fit the data for both measures. No significant improvement in the fit of the model was obtained by introducing assumptions about the dependence of lower respiratory illness on maternal or paternal smoking.

The major results of the log-linear analyses can be seen more clearly from Table 3, which shows the differences in the rates of lower respiratory illness between children of smoking mothers and children of non-smoking mothers over the three-year period. During the first year, children of smokers had rates of lower respiratory illness which were seven to 11 per 100 higher than for children of non-smokers; for the second year, this difference declined to five to six per 100; and by the third year the differences were clearly negligible (0 to 3 per 100).

The results for the first year of life show that there is a general and significant tendency for rates of lower respiratory illness to rise with maternal daily cigarette intake. However, because of the coarse grouping method used in Table 2, the nature of the relationship between cigarette intake and rates of illness is not clear. To provide a more sensitive analysis, the smoking behaviour of mothers was classified into six groups: non-smoker; one to five cigarettes a day; six to 10 cigarettes a day; 11 to 15 cigarettes a day; 16 to 20 cigarettes a day; and 21+ cigarettes a day. Using the median intake values for these groupings, logistic models were fitted to the rates of bronchitis/pneumonia and total lower respiratory symptoms. The results of this analysis are summarised in Figs. 1 and 2, which show the fitted dose/response curves and the observed data. While both models showed a satisfactory fit $(0·7 > p > 0·3)$ to the data as measured by the deviance statistic, it is clear that there is some discrepancy between the fitted values and the observed data points. In particular, both analyses show a general tendency for the observed results to be higher than the predicted results for the group of subjects reporting an intake in the range of six to 10 cigarettes a day. Disregarding this discrepancy, the results suggest that increases of
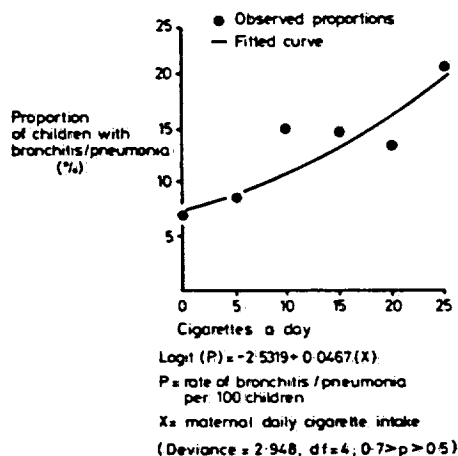
Fig. 1 *Dose/response curve between maternal daily cigarette intake and rates of bronchitis/pneumonia in the first year of life.*

Logit (P) = −2·5319 + 0·0467 (X)

P = rate of bronchitis/pneumonia per 100 children

X = maternal daily cigarette intake

(Deviance = 2·948, df = 4; 0·7 > p > 0·5)
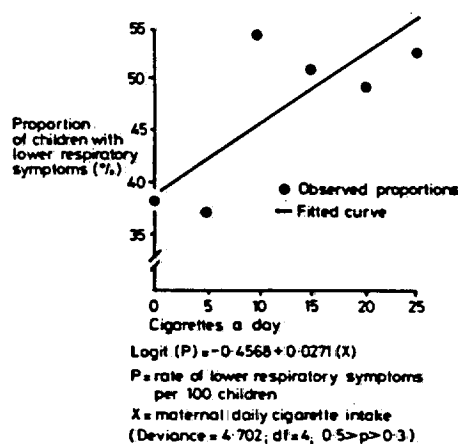
Fig. 2 *Dose/response curve between maternal daily cigarette intake and rates of lower respiratory symptoms in the first year of life.*

Logit (P) = −0·4568 + 0·0271 (X)

P = rate of lower respiratory symptoms per 100 children

X = maternal daily cigarette intake

(Deviance = 4·702; df = 4; 0·5 > p > 0·3)

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Table 4 *Comparison of slope coefficients of the unadjusted and adjusted fitted logistic curves*

| | BRONCHITIS/PNEUMONIA | | LOWER RESPIRATORY SYMPTOMS | |
	B	SE	B	SE
Unadjusted	0.0467	0.0112	0.0271	0.0076
Adjusted	0.0394	0.0118	0.0237	0.0081
	t = 0.45	p >0.05	t = 0.31	p >0.05

five cigarettes a day result in an approximate increase of 2·5–3·5 per 100 in the rates of lower respiratory illness.

However, the dose/response curves shown in Figs. 1 and 2 do not take into account the effect of other factors which may be correlated with both smoking and lower respiratory illness. To adjust the results for the possible effects of these factors, the data were re-analysed using logistic models in which maternal age, education, family size, and family living standards were introduced as additional factors. Table 4 gives a comparison of the B (slope) coefficients for the unadjusted and adjusted models. The results show that the effect of introducing the control factors is to reduce slightly the slope of the regressions. However, the differences between the adjusted and unadjusted slopes are not significant, indicating that the dose/response relationships depicted in Fig. 1 provide a good approximation to the relationships after the data have been adjusted for confounding factors.

Discussion

In confirmation of the findings of Colley *et al*[1] the correlation between parental smoking and childhood lower respiratory illness appeared to be most marked for the first year of life and showed a steady decline with increasing age. At one year, clear differences between the offspring of smokers and non-smokers were evident; at two years the evidence was equivocal; and by three years an association between maternal smoking and infant lower respiratory illness was clearly absent. However, these findings are not entirely consistent with reports[5-8] which have shown greater rates of respiratory problems (morning cough and breathlessness) among children of school age with smoking parents. One hypothesis which satisfies the available data is that the effect of parental smoking on childhood lower respiratory illness and symptoms is two-fold. During early life, and particularly the first year, prolonged contact with cigarette smoke would appear to precipitate or exacerbate lower respiratory illness in children; this effect is relatively short-lived and disappears at the age of about 2. However, prolonged exposure to cigarette smoke over a period of years may have a compound interest effect in compromising the

respiratory function of children, with the result that by the time middle childhood is reached, children of smokers have a greater rate of lower respiratory illness or symptoms.

For the first year of life, the fitted dose/response curves showed an almost linear tendency for rates of illness to increase with maternal smoking: increases of five cigarettes a day resulted in increases in rates of lower respiratory illness in the region of 2·5 to 3·5 incidents per 100 children at risk. However, the observed data showed a number of deviations from the smoothed dose/response function. For both measures of lower respiratory illness the observed rates of lower respiratory illness for women reporting an intake of six to 10 cigarettes a day were markedly higher than the rate estimated from the curve. This aberration in the results almost certainly reflects the effects of a reporting bias in the daily cigarette intake estimates, with women having a tendency to round their estimates down to the convenient and perhaps socially acceptable '10 a day'. Because of the possible biasses in maternal reports, the dose/response curves should be treated as providing only an approximate measure of the sensitivity of rates of infant lower respiratory illness to maternal smoking habits.

Reprints from Mr. D. M. Fergusson, the Christchurch Child Development Study, Department of Paediatrics, Christchurch Clinical School of Medicine, Christchurch Hospital, Christchurch, New Zealand.

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ABSTRACT. Recent studies have indicated higher rates of certain respiratory conditions among children who live in households with adults who smoke cigarettes. This paper analyzes data from the 1970 National Health Interview Survey. Children in families with no smokers had an average of 1.1 fewer restricted-activity days and 0.8 fewer bed-disability days per year than did children in families with two smokers. Children in families with one smoker were in between. Acute respiratory illness accounted for the difference in disability days among children in families with different smoking characteristics. Family smoking was also measured by the combined number of cigarettes smoked by adults; children in families which smoked 45 or more cigarettes a day had 1.9 more restricted activity days and 0.9 more bed-disability days due to acute respiratory conditions than did children in families who did not smoke cigarettes. The age of the child, the number of adults in the family, the education of the family head, and the family income were all controlled and did not eliminate the relationship between children's health and family smoking.

Children's Health in Families with Cigarette Smokers

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Abstract: Recent studies have indicated higher rates of certain respiratory conditions among children who live in households with adults who smoke ciga- rettes. This paper analyzes data from the 1970 National Health Interview Survey. Children in families with no smokers had an average of 1.1 fewer restricted-ac- tivity days and 0.8 fewer bed-disability days per year than did children in families with two smokers. Chil- dren in families with one smoker were in between. Acute respiratory illness accounted for the difference in disability days among children in families with dif- ferent smoking characteristics. Family smoking was also measured by the combined number of cigarettes smoked by adults; children in families which smoked 45 or more cigarettes a day had 1.9 more restricted activity days and 0.9 more bed-disability days due to acute respiratory conditions than did children in fami- lies who did not smoke cigarettes. The age of the child, the number of adults in the family, the education of the family head, and the family income, were all controlled and did not eliminate the relationship between chil- dren's health and family smoking. (Am J Public Health 1981; 71:290-293.)

Introduction

It has been fairly well accepted that a person's cigarette smoking is hazardous to his/her health. Recently there has been concern that cigarette smoking could adversely affect the health of nonsmokers exposed to the fumes.[1] If such a relationship exists it should manifest itself by comparing the health of children in smoking and nonsmoking families. Pre- vious studies have been inconsistent. Some have reported that children from families with smokers were less healthy than children from families with no smokers,[2-4] while others failed to uphold this relationship.[5] The National Health In- terview Survey (NHIS) provides a large national probability sample to test the relationship of children's health to ciga- rette smoking by adult family members, and this paper will report an analysis of NHIS data.

Materials and Methods

The 1970 National Health Interview Survey collected data about smoking and health characteristics from a proba- bility sample of about 37,000 households in the civilian, non- institutionalized population of the United States. Data were weighted to reflect the probability of selection, adjusted for household nonresponse, and further adjusted to reflect Unit- ed States Bureau of the Census population estimates for age- race-sex categories. Standard errors for most statistics were calculated using balanced, half-sample replication.[6] The multivariate analysis was made using the FUNCAT proce- dure of SAS (Statistical Analysis System),[6] with an adjust- ment for weighting and clustering of children in households approximating the method suggested by Choi.[7] Further de- tails of the survey, sample, and methods of estimation are available.[8]

Data were collected during personal interviews by per- sonnel of the US Bureau of the Census. Adult household members responded for themselves, for children, and for nonpresent adults. Data about smoking were collected for persons 17 years of age and over. Data about illness and in- jury during the two weeks prior to interview were collected for all ages.

Two measures of cigarette smoking in the child's envi- ronment were used: number of smokers 17 years and over, and number of cigarettes smoked by all persons 17 years and over, combined. It was assumed that the greater the number of smokers in the family, the greater the amount of cigarette smoke to which the child was exposed. Similarly, it was as- sumed that the greater the combined number of cigarettes smoked by the family, the greater the amount of cigarette smoke to which the child was exposed. Data on cigarette smoking for every family member 17 years and over were available for 98.5 per cent of the children in the study. Data on the number of cigarettes smoked for every adult family member were known for 95.2 per cent of the children. Chil- dren were excluded from the analysis if the smoking charac- teristic of any adult member was unknown.

Health of children was measured along two dimensions: effect of illness and type of illness. Total restricted-activity days were any days that children cut down on their usual activities for all or most of the day because of illness. Bed- disability days were a subset of total restricted-activity days in which the child stayed in bed for all or most of the day. All conditions included any acute illness, chronic illness, acci- dent, or injury that resulted in disability days. Acute respira- tory conditions included only those conditions with an onset within three months of interview and classifiable into the In-

TABLE 1—Per Cent of Children and Days of Disability by Type of Condition, by Smoking Characteristics of the Family: Children Under 17 Years of Age, United States, 1970

Smoking Characteristics of Family	Per Cent of Children	All Conditions		Due to Acute Respiratory Conditions		Not Due to Acute Respiratory Conditions	
		Total Restricted Activity Days	Bed Disability Days	Total Restricted Activity Days	Bed Disability Days	Total Restricted Activity Days	Bed Disability Days
All	100.0	9.4	4.4	4.5	2.3	4.9	2.0
Number of smokers 17 years and over							
None	37.8	9.1	4.0	4.1	2.1	4.9	2.0
1	37.4	9.3	4.4	4.4	2.4	4.9	2.1
2 or more	24.8	10.2	4.8	5.3	2.7	4.8	2.1
Average Number of Cigarettes per Day							
Less than 1	39.3	9.1	4.1	4.1	2.1	4.9	2.0
1-14	13.7	8.7	4.4	4.2	2.4	4.5	2.0
15-24	18.6	9.2	4.6	4.4	2.4	4.7	2.2
25-34	8.5	11.2	5.5	5.7	3.1	5.5	2.4
35-44	10.0	9.7	3.7	4.2	1.9	5.6	1.8
45 or more	9.9	10.6	5.2	6.0	3.0	4.5	2.1

ternational Classification of Disease" code numbers 460–486, 501, 508–516, 519 and 783, but excluded certain conditions always considered chronic (e.g., asthma, hay fever, tuberculosis, repeated attacks of sinus trouble, and allergy). Respiratory conditions have been most often linked with cigarette smoking and constitute a substantial portion of the illnesses of all children. It was expected that family smoking would show a greater relationship to acute respiratory illness among children than to other types of illness.

Results

In 1970, 37.8 per cent of children 0–16 years old lived in families with no adult smokers, 37.4 per cent lived in families with one smoker, and 24.8 per cent lived in families with two or more smokers. Table 1 shows that the average number of restricted-activity days per year increased with the number of adult smokers in the family. The difference of 1.1 days a year between children in non-smoking families and children in two- or more-smoker families (t = 2.85) supports the hypothesis that family smoking adversely affects the child's health. A similar relationship was found for bed-disability days. Children in two- or more-smoker families spent an average of 0.8 more days in bed each year than did children in non-smoking families (t = 3.10).

As was hypothesized, acute respiratory illness showed a greater relationship with family smoking than did other conditions. Children in two- or more-smoker households averaged 1.2 more days of restricted-activity due to acute respiratory conditions than children in non-smoking families (t = 4.41). There was no difference in the number of restricted-activity days due to conditions other than acute respiratory between children with differing numbers of smokers in their families. Similarly, family smoking was related to differences in bed-disability due to acute respiratory conditions but not to bed-disability due to other types of conditions.

In 1970, 39.3 per cent of children lived in families where no one smoked or where smoking was rare enough to average less than one cigarette a day among all adult members combined. At the opposite end, 9.9 per cent of children lived in families that smoked 45 or more cigarettes combined. The number of cigarettes smoked had a less consistent relationship with children's health than did the number of smokers. Although the number of total restricted-activity days did not uniformly increase with increased family smoking, children from families where 45 or more cigarettes were smoked each day had 1.5 more restricted-activity days than did children from families that smoked less than one cigarette per day (t = 2.73).

Bed-disability days of children showed an increase with family smoking except for the anomalies at 25-34 and 35–44 cigarettes. When only acute health conditions were considered, the relationship of children's health and adult smoking was more consistent. Children in families smoking 25-34 cigarettes a day still showed a higher rate of illness than would be expected if there were a continuous increase, and those in families smoking 35–44 cigarettes had a lower rate of illness. Even with those exceptions to the hypothesized pattern, it was generally found that the more cigarettes smoked by the family, the more days of illness the child had. However, the relationship was only noticed for acute respiratory conditions and not for other types of illness.

For both measures of illness—restricted-activity days and bed-disability days—for all conditions and for acute respiratory conditions, there were greater differences in illness by family smoking when smoking was measured by the number of cigarettes per day than by the number of smokers.

Smoking is related to many factors, and perhaps some of the relationships observed between smoking and children's illness was due to smoking and illness being related to the same external factors. Age of the child, number of adults in the household, family income and education of the head

TABLE 2—Average Number of Restricted-Activity Days Due to Acute Conditions by Number of Adult Smokers in the Family, by Selected Characteristics of the Child or Family: Children under 17 Years of Age, United States, 1970

Characteristics of Child or Family	Number of Children		Number of Smokers 17 Years and Over			
	Population Estimate (000)	Sample	Total[a]	None	1	2 or more
All[b]	86,711	39,791	4.5	4.1	4.4	5.3
Age of Child (years)						
Under 6	21,682	12,675	5.8	5.4	5.7	6.7
6-11	24,756	14,810	4.0	3.7	3.7	5.0
12-16	20,272	12,306	3.7	3.2	3.9	4.3
Number of Persons 17 Years and Over						
1	6,788	3,979	4.8	5.8	3.9	...
2	43,830	26,095	4.5	4.0	4.4	5.6
3 or more	15,974	9,674	4.3	3.1	4.8	4.8
Family Income						
Under $5,000	11,259	6,675	4.8	5.2	4.5	5.5
$5,000-$9,999	24,139	14,438	4.3	3.7	3.9	5.7
$10,000-$14,999	17,233	10,241	4.6	4.4	4.7	4.8
$15,000 or more	9,772	5,890	4.5	3.2	5.3	5.4
Education of Head						
0-11 years	26,530	15,842	4.5	3.7	4.4	5.3
12 years	22,326	13,397	4.4	4.4	3.9	5.4
13 or more years	16,937	10,022	4.7	4.2	5.1	5.4

[a]Includes children where smoking status of a household adult was unknown

[b]Includes children where family income or education of the head was unknown, or where there was no family member 17 years of age or over

were all examined (see Table 2) to see if they affected the relationship between adult smoking and child health. Only one measure of health and one of illness was used (average number of restricted-activity days due to acute conditions), but the same results would be expected from the other measures. Age of the child did not affect the direct relationship between restricted-activity days and the number of smokers in the household. The relationship also held for households having two adults and for households with three or more adults. For the one adult households, the relationship differed, with 5.8 restricted-activity days due to acute respiratory conditions for children in nonsmoking one-adult households and 3.9 days for children in smoking one-adult households.

The relationship of more smokers in the household with more restricted-activity days due to acute respiratory conditions was observed at most levels of family income and education of the head. The exceptions were for children whose family incomes were less than $5,000 and children whose family heads graduated from high school, among whom fewer restricted-activity days were observed where there was one smoker than when there were none.

Controlling for a number of background variables individually did not eliminate the relationship of household smoking and children's health. A log-linear model for categoric data analysis was used to simultaneously control for all the variables. Table 3 shows that the numbers of cigarette smoking adults in the family had a significant relationship with whether or not the child was restricted in activity due to illness in the preceding two weeks independent of the other characteristics. The additive model fit sufficiently well that interaction terms were not included.

Discussion

Analysis of data from the 1970 National Health Interview Survey found that children in households with adult cigarette smokers had more days of total restricted-activity and bed-disability than did children in households with no smokers. In general, the more cigarettes smoked, the greater the days of illness. The differences in disability days were due to acute respiratory disease, and could not be explained by differences in children's ages, family income, education of the family head, or the number of adults in the household.

The few anomalies in the data do not invalidate the general hypothesis. The high illness associated with children of families smoking 25-34 cigarettes a day was observed for conditions other than acute respiratory and therefore may have nothing to do with the level of smoking. The low level of illness of children from families smoking 35-44 cigarettes a day may also indicate some type of statistical artifact. If a single grouping of 25-44 cigarettes were made, the number of total restricted-activity days due to acute respiratory conditions would be 4.9 with the number of bed-disability days 2.5. These figures fit nicely into the hypothesized relationship of increasing illness with increasing family smoking. In Table 2, all the figures that did not fit the hypothesis were in the one-smoker column. The low level of illness for the one-

TABLE 3—Chi-square Values for the Independent Additive Effects by Source on Restricted Activity of the Child in the Previous Two Weeks by Source of Effect

Source	Degrees of Freedom	Unadjusted Chi-square		Adjusted Chi-square	
		Unweighted	Weighted	Unweighted	Weighted
Intercept	1	7067.25	10,854,936	3533.63*	3236.42*
# of Smokers	2	13.34	23,827	6.67*	7.10*
Education of Head	2	44.90	93,826	22.45*	27.97*
Family Income	3	7.28	13,884	3.64	4.13
# of Adults	2	2.59	13,956	1.29	4.16
Age of Child	2	3.72	1,893	1.36	0.50
Residual	271	1.91	560,148	—	—

*Significant at the 0.05 level

smoker families was most prominent in the single adult families. Smoking single adult families might be sufficiently different from nonsmoking single adult families in demographic characteristics related to health of children to give rise to the observed relationship.

The mechanism for the relationship between adult smoking and child health was not investigated. The cigarette smoking of adults could directly affect the susceptibility of the children to respiratory disease by decreasing their lung functioning. Cigarette smoking by adults could also affect children's health by increasing the children's contact with disease if the smokers themselves have a higher incidence of disease. Speizer, et al, found clustering of respiratory illness among household members, but found smoking was greater in households without clustering of illness.[10] Lebowitz and Burrows found that while respiratory symptoms in children were related to smoking habits of adults in the household, the relationship did not hold when symptoms in adults were controlled.[5] On the other hand, Tager, et al, found an inverse dose-response relationship between pulmonary function of children and the number of smoking parents in the household.[2,3] The findings of this paper do not suggest the mechanism of the effect, but do support the hypothesis that there is an effect.

It could be that adult smoking increases the probability of the child smoking, and it is the smoking of the child rather than the adult that affects the child's health. Tager, et al, found that the effect on the pulmonary function of children was predominantly due to parental smoking and was independent of the use of cigarettes by children.[3] Smoking of children was not measured in the National Health Interview Survey, but the age of the child was found to have no effect on the relationship of adult smoking and child health. If it were the child's smoking that affected health, there would only be a relationship between adult smoking and older children's health. The data showed a relationship for all three age groupings of children, being at least as strong among children under age 6 as among children 13–16 years of age.

Other factors that could have a relationship with children's health and with adult smoking were not investigated. For example, if children in rural areas spend more time outdoors, they might not be as affected by adult smoking. This would not mitigate the relationship discussed in this report, however, and might strengthen the observed relationship if

controlled. In a preliminary analysis, the size of the urban area was found to have no effect on the relationship between the number of adult smokers and restricted-activity days in children and was investigated no further.

This study, using cross-sectional data, offers no direct proof that adult smoking adversely affects children's health. However, the findings from this large, representative, national household survey suggest a causal relationship. A number of factors which could have given rise to a spurious relationship were controlled and not found to eliminate the relationship. The data support the findings of others that cigarette smoking by adults adversely affects the health of children in their families.

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Love, G.J., Lan, S.P., Shy, C.M., Struba, R.J. "The Incidence and Severity of Acute Respiratory Illness in Families Exposed to Different Levels of Air Pollution, New York Metropolitan Area, 1971-1972" Archives of Environmental Health 36(2): 66-74, 1981.

ABSTRACT: The incidence and severity of acute respiratory disease was studied in families in three New York communities with different ambient levels of SO_2 and particulate air pollution. Upper, lower, and total respiratory disease rates in fathers, mothers, and school children tended to be higher in the communities with higher pollution levels. Similar higher rates, however, were not observed among preschool children. Regression analyses were used to adjust rates for socioeconomic status, parental smoking, chronic bronchitis in parents, and possible indoor pollution resulting from the use of a gas stove for cooking. After these adjustments the community differences were still significant ($P < .01$), for schoolchildren. The indoor pollution related to gas stoves was a significant covariant among children. The effects of smoking were inconsistent. It was not possible to attribute the higher rates observed to any specific pollutant, since both SO_2 and particulate matter levels were higher in the high pollution communities, nor was it possible to attribute the excesses to current levels of exposure or to a residual effect of previous higher exposure concentrations. The fact that young children did not follow the pattern suggests the latter. It was concluded, however, that current or previous exposures to the complexity of air pollutants in New York City was at least partially responsible for increased incidences of acute respiratory disease.

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The Incidence and Severity of Acute Respiratory Illness in Families Exposed to Different Levels of Air Pollution, New York Metropolitan Area, 1971-1972

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ABSTRACT. The incidence and severity of acute respiratory disease was studied in families in three New York communities with different ambient levels of SO_2 and particulate air pollution. Upper, lower, and total respiratory disease rates in fathers, mothers, and school children tended to be higher in the communities with higher pollution levels. Similar higher rates, however, were not observed among preschool children. Regression analyses were used to adjust rates for socioeconomic status, parental smoking, chronic bronchitis in parents, and possible indoor pollution resulting from the use of a gas stove for cooking. After these adjustments the community differences were still significant ($P < .01$), for schoolchildren. The indoor pollution related to gas stoves was a significant covariate among children. The effects of smoking were inconsistent. It was not possible to attribute the higher rates observed to any specific pollutant, since both SO_2 and particulate matter levels were higher in the high pollution communities, nor was it possible to attribute the excesses to current levels of exposure or to a residual effect of previous higher exposure concentrations. The fact that young children did not follow the pattern suggests the latter. It was concluded, however, that current or previous exposures to the complexity of air pollutants in New York City was at least partially responsible for increased incidences of acute respiratory disease.

THE INCIDENCE AND SEVERITY of acute respiratory disease was studied in New York families exposed to different concentrations of air pollution during the 1971-1972 school year. The study concentrated on respiratory infections because their high incidence and associated disability ranked them as a major public health problem.[1] A number of studies in different parts of the world have shown an association between the incidence of acute

respiratory disease (ARD) and exposure to elevated concentrations of ambient air pollution.

In England the incidence of ARD was found to be associated with weekly maximum concentrations of sulfur dioxide (SO_2) and smoke,[2] (the peak 24-hr mean concentrations of both pollutants often exceeded 750 $\mu g/m^3$ and were thus higher than those occurring since 1970 in the US) and in France, daily variations in SO_2, smoke, and temperature were all observed to be associated with the onset of ARD in workers,[3] although temperature appeared to be the most important of these three exposure variables. In Ontario, Canada, hospital admissions for ARD were significantly correlated over a 12-month period with an index of ambient air pollution based on measured concentrations of SO_2 and particulate.[4] This association remained after adjustment for the effects of temperature. It was not possible to separate the impact of SO_2 or particulates in any of these investigations, as illness was correlated with both factors.

Several studies have shown associations between air pollution concentration and ARD in children. Douglas and Waller[5] and Lunn et al.[6] found higher incidences of LRD in children living in more polluted areas of England and Wales, respectively. In the latter study, rates of upper respiratory disease (URD) also were increased. Both of these investigations provided evidence of the importance of socioeconomic status as a potential confounding factor in such studies. Again, neither of the investigations provided sufficient aerometric data to permit evaluation of specific types or concentrations of pollutants associated with the increased illness rates. A second study by Lunn et al.,[7] after a 4-yr period of improving air quality, showed that the differences in the incidence of respiratory illness were no longer significant.

In the United States, rates of ARD and days of restricted activity,[8] and rates of lower respiratory disease (LRD)[9] were shown to be positively associated with measured annual mean levels of total suspended particulates (TSP), suspended sulfate (SS), and SO_2. Hammer et al.[10] studied retrospectively the occurrence of acute lower respiratory disease in children 1-12 yr of age residing in the same communities used in the investigation reported here. These authors found higher rates of croup, bronchitis, and "any lower respiratory disease" among white and black children residing in communities with higher concentrations of particulate matter, SO_2, and suspended sulfate. Difference in family size, crowding, parental smoking, and use of gas stoves for cooking could not explain the excesses. Other studies in the United States found high correlations between the incidence of respiratory illness lasting 7 days or more among female industrial workers and sulfation rates,[11,12] and associations between daily absence rates among white collar workers and daily pollution concentrations.[13] Higher rates of respiratory illness were also observed in children and parents living in an area with high NO_2 pollution,[14,15] although no association was found between weekly absence rates among elementary school pupils and weekly mean oxidant concentration.[16]

Previous studies have reported increases in ARD, particularly LRD, to be associated with exposure to elevated ambient concentrations of SO_2 and particulates, but have been unable to attribute the increases specifically to either pollutant. In most instances, the concentrations exceeded those that frequently occur in metropolitan areas of the United States today. More recent studies have, however, suggested that some fractions of the TSP, possibly suspended sulfate, may be more important than either SO_2 or TSP.

The current study was undertaken by the U.S. Environmental Protection Agency in 1971 as part of a major effort to provide information relevant to the adequacy of Air Quality Standards. Publication of the information has been delayed because, after lengthy consideration, it was determined by the regulatory agency that analysis and interpretation of the data collected should be done by an independent group. The relevance of the data has not diminished in the interim, however, since few, if any, similar studies have been undertaken since, and because air quality standards have continued to be a controversial topic among scientists, industrialists, and environmentalists. In addition, current pressures to curtail the dependence of the United States on foreign sources of oil tend to intensify the need to review all available information concerning the potential impact of possible alternatives.

There are two objectives of the present study: (1) to test the hypothesis that the frequency and/or severity of ARD would be higher in more polluted communities, and (2) to investigate the importance of other known covariables—singly and in combination. These include socioeconomic status, as indicated by educational attainment of the head of the household or crowding in the home, as well as smoking, the presence of chronic bronchitis in parents, and the use of gas stoves.

METHODS AND MATERIALS

Selection of study communities and participants. Two New York City metropolitan communities—the Westchester section of Bronx and the Howard Beach section of Queens—were selected to represent areas with pollution resulting from both urbanization and industrialization, as these had significant concentrations of both TSP and SO_2. Riverhead, an eastern Long Island town, was chosen as a "low" pollution comparison community. Aerometric data gathered in 1970, showed that collectively, these three communities formed a pollution "gradient" with respect to particulate matter and SO_2.

Families were recruited in each area to participate in a prospective study of acute respiratory illness. Classroom lists from individual public elementary schools identified candidate families and provided addresses. Each family from these lists was requested to participate, and when agreement was obtained, a questionnaire pertaining to demographic and personal characteristics was administered. Refusal rates were very low (< 5%), although accurate documentation was not maintained. The only restrictions placed on the selection of families were (a) each must have had at least one child in elementary school, (b) must have lived within 2.4 km of an air monitoring station, (c) have lived at the same address for at least 1 yr, (d) have no plans for moving during the subsequent year, and (e) have a telephone in the home. Approximately 250 families were recruited in each area during the summer of 1971. Some

of the families had also participated in a previous EPA study of ARD.[11]

Assessment of air pollution exposure. Monitoring sites were located on the tops of buildings approximately 10 m above ground level. This was done to provide for continuity with determinations of exposure in previous EPA studies in these areas.[11] The New York City Department of Air Resources was also monitoring pollutants at the same sites, which provided useful data for comparative purposes.

Daily 24-hr samples were collected at each site for total particulate matter (TSP) in high volume samplers; respirable particulate matter [RSP (defined as particles with a diameter $\leq 3.5 \mu m$)] in cyclone separators; and SO_2 in bubblers analyzed by a modified West-Gaeke method. Strips of the high-volume filters were used to determine concentrations of water soluble sulfates (turbidimetric method employing a spectrophotometer) and water soluble nitrates (automated colometric method).

Collection of health data. Prior to the initiation of the study, interviewers were selected and given 2 or 3 days of intensive training in methods to solicit information by telephone. Throughout the study, interviewers were monitored regularly by the supervisor to insure that techniques were not altered; interviewers were rotated among the study subjects so that only on rare occasions was a family contacted by the same interviewer two consecutive times.

Beginning in October 1971 and continuing for 16 consecutive 2-wk periods, interviewers contacted each family by telephone biweekly to ask about acute respiratory illness experienced during the previous 2 wk. Whenever possible, information was obtained from the mother or guardian, but on some occasions, the next of kin was queried. Accurate documentation was not maintained, but it is estimated that the frequency with which someone other than the mother provided information represented < 2% of the interviews. During the interview, the following information was collected for each member of the family: (a) any new illness, (b) fever, (c) respiratory involvement, (d) days of restriction of normal activity, (e) physician consultation, (f) physician diagnosis of an ear infection, and (g) day of onset of symptoms. Each reported disease was classified as upper respiratory disease (URD) if symptoms were limited to head cold, sinus or post-nasal drip, runny nose, sore throat, or dry, nonproductive cough. The lower respiratory disease (LRD) classification was assigned whenever symptoms included bronchitis, pneumonia, croup, chest cold, productive cough, or asthmatic symptoms.

The information requested pertained to asthmatic symptoms because it was believed that it would be understood better than "wheezing." Since any individual reported initially to be an asthmatic was eliminated from the analysis, it is not believed that this question could have biased the results seriously. None of the illnesses were verified clinically. The reliability of the data collected was verified once via a second interviewing of a random sample of families several days after the original call. The same questions were asked at these re-interviews by an interviewer who had not contacted the family previously.

Data analysis. The first 2-wk study period was treated as a developmental activity and data were not included in the study. Only families who participated for 7 or more

of the remaining 15 study periods were considered in the analysis; this group was further divided into residentially stable and mobile families. A stable family was defined arbitrarily as one living at the same residence for at least 5 yr. Analyses were limited further to the white families, since the percentages of non-whites varied from area to area. Comparisons were then made among the three communities of URD and LRD rates per 100 person weeks for observations of fathers, mothers, and preschool (age 0-5) and elementary (age 6-12) school children. An illness ratio was derived for each individual as: (number of illnesses reported/number of weeks of participation) X 100 = illness rate per 100 person weeks. Each individual had three disease indicators: lower respiratory illness rate, upper respiratory illness rate, and all respiratory illness rate. These individual illness rates were used as the dependent variable in multiple-linear regression analyses.

Illness rates for groups were obtained by averaging the illness rates for all individuals within the group. Statistical significance of the group differences were determined by standard t tests. The average number of days of restricted activity, as well as the percent of illnesses prompting physician visits, were also compared.

Other factors that might affect the incidence of respiratory illness were considered in the analyses, including smoking habits of parents, crowding, educational status, bronchitis in parents, and use of gas stoves. The importance of these factors was assessed by stratification and by the use of multiple linear regression analysis.

In the multiple regression analysis, a square root transformation was made for the illness rates—to meet more adequately the statistical assumptions. Indicator (or dummy) variables were developed for the independent variables, including community, education, crowding, gas stove, smoking, and bronchitis. Analysis of variance tables were constructed to evaluate the effect of each of the independent variables on the illness rates. The interaction terms of smoking X bronchitis, and smoking X crowding also were examined for their significance. These variables were tested by the sequential F test, with the community effect as the last variable to be entered in the model. The other variables were entered in the following order: education, crowding, gas stove, smoking, bronchitis, smoking X bronchitis, and smoking X crowding. The significance level for the rejection of null hypotheses was set at .01 (i.e., $\alpha = .01$).

The distribution of illness rates are inherently skewed to the left. But, the analysis of variance through multiple regression method used in this study is robust because a Fixed Effect Model was adopted, and the sample sizes for the communities were large and approximately equal. The square root transformation tended to reduce the effect due to tail-end cases. For a detailed discussion, see Neter and Wasserman[17] and Kempthrone.[18]

RESULTS

Air pollution exposure concentrations. Among the three study areas, the Riverhead populations were exposed to lower concentrations of all pollutants than were those in Howard Beach and Westchester. Annual mean concentrations of TSP, as indicated by the EPA measurements, were about 40% of the ambient annual air quality standard of

Table 1.—Measurements* of Suspended Particulate and SO₂ Air Pollution in 1971 and 1972

TSP	1971 Annual Geometric Mean†	1971 Percentiles of 24-hr Means 90th	1971 Percentiles of 24-hr Means 95th	1972 Annual Geometric Mean	1972 Percentiles of 24-hr Means 90th	1972 Percentiles of 24-hr Means 95th
Riverhead	30.6	55.4	64.1	32.1	59.2	70.1
Howard Beach	56.0	101.3	115.5	55.3	91.1	109.0
Westchester	76.4	138.6	168.8	78.7	150.4	170.7
RSP†						
Riverhead	23.2	68.3	77.5	21.5	52.6	60.7
Howard Beach	32.6	66.5	72.8	26.4	58.1	70.3
Westchester	42.6	76.8	88.5	34.3	72.6	85.4
SS						
Riverhead	8.5	18.2	22.8	8.4	19.2	22.8
Howard Beach	11.6	21.9	29.2	11.0	21.5	26.6
Westchester	12.5	24.7	31.6	11.4	23.3	28.6
SN						
Riverhead	1.3	3.8	5.0	1.0	3.0	4.1
Howard Beach	2.6	6.8	8.9	1.8	5.2	7.3
Westchester	2.9	8.1	11.3	1.9	5.2	6.9
SO₂						
Riverhead	22.8‡	53.3	73.5	21.6‡	34.6	71.8
Howard Beach	34.7‡	104.3	121.3	37.5‡	73.8	99.9
Westchester	51.4‡	124.4	154.7	49.5‡	104.6	147.8

NOTES: TSP = total suspended particulates; RSP = respirable suspended particulates; SS = suspended sulfates; and SN = suspended nitrates.
*Measurements expressed as $\mu g/m^3$.
†RSP data in 1971 are for July to December only.
‡Annual arithmetic mean.

75 $\mu g/m^3$ in Riverhead; 76% of the standard in Howard Beach; and slightly exceeded this standard in Westchester (Table 1). Data collected by the New York City Department of Air Pollution Control suggest that these measurements may have systematically underestimated the actual ambient exposures by 10-30%. This difference is also in agreement with the findings of a Congressional Investigative Committee.[19] The sulfate and nitrate measurements were also subject to similar (but smaller) errors of undermeasurement. Table 1 also displays 90th and 95th percentile concentrations, which show that populations were sometimes exposed to significantly higher concentrations of these materials than the mean values would indicate.

The concentrations of RSP, suspended sulfate, and suspended nitrate, generally followed the same gradient as did TSP; in 1971, however, the indicated 90th and 95th percentiles for RSP in Riverhead exceeded those in Howard Beach (Table 1). Exposure to particulate pollution is likely to be overestimated for Westchester residents because the monitoring station for this area was located in a commercial area having heavy motor vehicle traffic, while study participants lived in the adjacent residential neighborhood with less traffic. The Howard Beach and Riverhead monitoring stations were situated in residential areas.

Annual mean concentrations of SO₂ (Table 1) were about 22 $\mu g/m^3$ in Riverhead, 35 $\mu g/m^3$ in Howard Beach, and 50 $\mu g/m^3$ in Westchester—still evident of an exposure gradient—but only 28%, 44%, and 63%, respectively, of the annual air quality standard for SO₂ of 80 $\mu g/m^3$. Measurements of NO₂ made in 1974 by an accepted method (arsenite) suggested that none of the concentrations exceed the annual air quality standard of 100 $\mu g/m^3$.

Demographic and personal characteristics of study populations. United States Census data for 1970 indicated that there were differences in the source populations from which the study groups were drawn. Median annual income for the Riverhead census tracts was < $10,000; about $11,000 for Westchester, and > $12,000 for Howard Beach. Non-white individuals constituted 9% of the Riverhead population, 5% in Howard Beach, and only 1% in Westchester. In Riverhead, Howard Beach, and Westchester, 54%, 48%, and 61%, respectively, of the source population older than 24-yr of age, had less than high school education. The specific study population showed similar differ-

Table 2.—Characteristics of Stable Families Only in Study Population

	Percentages of Household Study Population		
	Riverhead	Howard Beach	Westchester
More than one person per room	21	10	26
Head of household with less than high school education	30	23	36
Gas stove for cooking	64	96	99
Cigarette smokers: Mothers	35	42	44
Fathers	44	45	47
White	79	99	98

ences in the characteristics measured, but usually of less magnitude (Table 2). These differences are adjusted for in the analyses, or are controlled by limiting the study group to members of white stable families who were reported to have no asthma, heart or lung disease, and who reported no extensive occupational exposure to dust. These selection procedures limited the study populations to 42%, 47%, and 49% of the candidate study populations in Riverhead,

Fig. 1. Respiratory illness rates per 100 person weeks of observation in white stable families exposed to different levels of air pollution.

Howard Beach, and Westchester, respectively.

Among the 1982 study subjects included in the analysis, average participation during 15 2-wk study periods was more than 97%. Participation exceeded 90% for each study period.

Illness frequency and severity. In a reliability check for illness reporting, 95.3% of an original sample of 1,035 individuals was reinterviewed. In this second interview, 2 of the 64 families originally reporting a new illness, now reported no new illness, and none of the negative replies were changed, thus yielding a concordance of 99.6%.

With only minor exceptions, higher rates of respiratory illness were reported for each family segment in Westchester and Howard Beach, than for those in Riverhead (Fig. 1). In most instances the rates for Howard Beach were higher than those in Westchester, and did not conform to the indicated pollution gradient. A larger percentage of the ARD episodes in Howard Beach and Westchester reported a physician visit than did those in Riverhead, suggesting that the residents of the higher pollution areas, in addition to experiencing more illness episodes, also more often felt that an episode was serious enough to warrant an examination by a physician. In Riverhead, the percentage of total ARD associated with physician visits ranged from 7.62 for mothers to 17.59 for preschool children. The combined data from Howard Beach and Westchester indicated that the percentage for individual family segments ranged from 4.94 to 8.40% higher than those in Riverhead.

The percentages of the various population segments experiencing no respiratory illness were consistently higher in the low pollution area, and the percentages experiencing more than two illnesses during the study period were consistently lower in the low pollution area. The occurrence of smoking or chronic bronchitis in parents was not associated consistently with higher rates of respiratory illness in children.
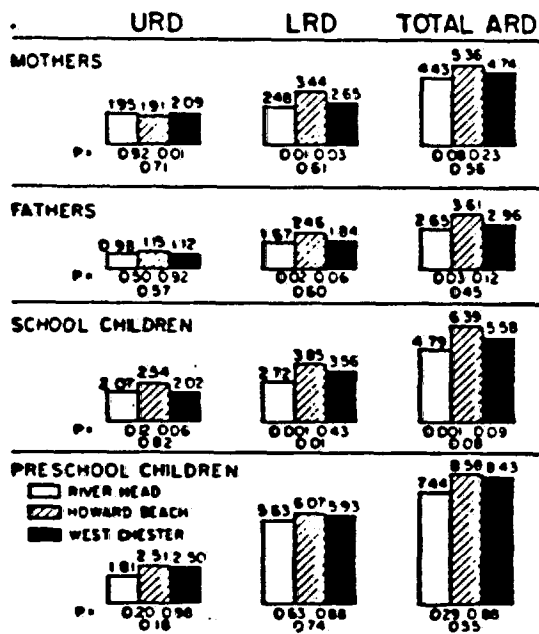
Table 3.—Multiple Linear Regression of Rates of URD, LRD and Total ARD on Education, Crowding, Smoking, Bronchitis, Gas Cooking, and Residence among Mothers, Fathers, School Children, and Preschool Children in New York, 1971-1972

Main Effect	df	F Values		Total ARD
		URD	LRD	
Mothers				
Regression*	7,473	1.04	2.42	3.14†
Education	1,473	5.83	6.00	13.45†
Crowding	1,473	0.57	0.30	0.01
Gas stove	1,473	0.44	0.24	0.01
Smoking	1,473	0.22	0.02	0.01
Bronchitis	1,473	0.60	4.41	3.99
Riverhead vs. Howard Beach	1,473	0.15	2.38	2.72
Riverhead vs. Westchester	1,473	0.59	0.28	1.04
Howard Beach vs. Westchester	1,473	0.36	0.94	0.25
Fathers				
Regression*	7,455	2.03	3.56†	4.77†
Education	1,455	4.32	14.03†	18.67†
Crowding	1,455	0.80	0.18	0.76
Gas stove	1,455	0.29	0.01	0.06
Smoking	1,455	7.91†	0.04	2.86
Bronchitis	1,455	1.03	4.61	4.35
Riverhead vs. Howard Beach	1,455	0.24	3.25	4.91
Riverhead vs. Westchester	1,455	0.11	0.32	0.91
Howard Beach vs. Westchester	1,455	0.01	2.01	1.85
School Children				
Regression*	7,811	4.27†	7.87†	9.42†
Education	1,811	7.86†	21.17†	25.09†
Crowding	1,811	1.19	7.65†	5.69
Gas stove	1,811	6.26	1.34	4.84
Smoking	1,811	0.10	4.23	2.66
Bronchitis	1,811	4.52	0.10	1.17
Riverhead vs. Howard Beach	1,811	8.77†	13.49†	21.21†
Riverhead vs. Westchester	1,811	4.54	15.38†	15.26†
Howard Beach vs. Westchester	1,811	0.43	0.24	0.55
Preschool Children				
Regression*	7,211	3.71†	2.56	4.97†
Education	1,211	0.05	1.84	2.21
Crowding	1,211	16.27†	0.64	7.67
Gas stove	1,211	1.13	6.57	9.21†
Smoking	1,211	0.01	0.36	0.63
Bronchitis	1,211	1.89	5.28	6.10
Riverhead vs. Howard Beach	1,211	0.13	0.43	0.05
Riverhead vs. Westchester	1,211	2.15	0.26	0.22
Howard Beach vs. Westchester	1,211	1.03	0.02	0.38

*Significance indicates an adequate fit of the model.
†Significant at .01 level (for 7 df, $F \geq 2.73$, for 1 df, $F \geq 6.76$).

Table 3 provides the results of the multiple linear regression of the rates of upper and lower ARD on education, crowding, smoking (or parental smoking), bronchitis (or parental bronchitis), gas stove, and residence (Riverhead vs. Howard Beach, Riverhead vs. Westchester, and Howard Beach vs. Westchester) among the four groups of study individuals: mothers, fathers, school, and preschool children. Inclusion of interaction terms had very little effect on the indicated association of higher illness rates with Howard Beach and Westchester. In addition, the community effect changed very little when it was determined before or after controlling for the effect of the other factors. As indicated by the significance of the F value for the overall regression, the model seems adequately fitted to the data. Educational attainment was an important factor in determining ARD rates ($P < .01$). Crowding appeared as an important factor among children, especially for LRD among school children and for URD among preschool

children. Smoking in the family was shown to be a significant variable at the $P < .01$ level only for URD in fathers. Use of gas stoves for cooking was associated with significant ($P < .01$) increases in total ARD in preschool children, but since the number of families without gas stoves in Howard Beach and Westchester was very small, this contrast must apply almost exclusively to the Riverhead population. Statistically significant ($P < .01$) increases in illnesses in Howard Beach or Westchester, when compared with Riverhead, were found only among the school children. Among this group, both Howard Beach and Westchester had significantly more LRD and total ARD. In Howard Beach significantly more URD was observed as well.

The relative ARD attack rates derived after adjusting for the effect of education, crowding, smoking, bronchitis, in parents, and the use of gas stoves for cooking (Table 4) agreed, in general, with the unadjusted data, except for the preschool children. More frequent illness among the other population segments is associated with residence in the more polluted areas. The higher rates in Howard Beach than in Westchester remain, but the magnitude of the differences is greatly reduced among schoolchildren.

DISCUSSION

The results support the hypothesis of an air pollution effect to the extent that incidence rates of ARD were lower in Riverhead, the low pollution area. The data confirmed the results of the earlier study of ARD in New York[3] in which higher illness rates were typically observed in Howard Beach and Westchester. Although most aerometric measurements suggested that pollutant concentrations were somewhat higher in Westchester than in Howard Beach, ARD rates did not follow this gradient.

The differences observed in the present study are of less magnitude than those found one year earlier and could represent an improvement in health status associated with improving air quality. It seems more likely, however, that the primary source of difference is the more conservative analysis method used for this report. The one argument that might be made for the possible effects of improved air quality is seen in the rates for preschool children (Table 4). This group historically was exposed to less pollution than were their older siblings, and the possible benefit may be observed in the lower adjusted ARD rates for this group in Howard Beach and Westchester than in Riverhead. This represents a distinct contrast to the relative attack rates for the other population segments. The results of the prospective study reported here, and the one conducted a year earlier, are in agreement with the retrospective study of Hammer et al.[9] that showed higher rates of LRD to have occurred in the higher pollution areas from 1969 through 1971.

Associations between air pollution and ARD might be affected both by the intensity of the exposure concentrations, which must vary considerably among the individuals of a study population, and by the inherent susceptibility of each individual included in the population. The data collected for this study suggest that in the high pollution areas, not only did the more susceptible individuals experience more frequent illnesses, but that some factor—pos-

sibly air pollution—increased susceptibility in a general manner, so that increased percentages of the populations experienced at least one illness.

It is possible that physician visits could relate more to economic factors than to illness severity; however, it is believed that the selection of the specific study populations minimized this potential bias. In this regard, higher reported illness rates are frequently associated with higher socioeconomic status, particularly as indicated by greater educational attainment of the head of household, a fair indicator of economic status. Riverhead ranked intermediate to Howard Beach and Westchester in this respect, indicating no significantly lower economic status for the Riverhead study group.

The location of the air monitoring station adjacent to a roadway with heavy traffic could have increased the quantities of air pollution (particularly TSP) collected at the Westchester site and explain to some extent why illness rates did not follow the indicated pollution gradient. Data to support this speculation are not available, however.

Factors other than air pollution that might have influenced the incidence of respiratory illness were examined. These included smoking, other indoor pollution, occupation, socioeconomic status, climate, and bronchitis in parents.

Smoking in the family was not identified as an important variable, but was controlled in the regression analysis. Other indoor pollution, possibly NO_2 produced by the combustion of gas in cooking stoves might have caused

Table 4.—Relative ARD Attack Rates Derived after Adjustment for Education, Crowding, Smoking, Bronchitis in Parents and Use of Gas Stoves

	URD	LRD	Total ARD
Mothers			
Riverhead	1.00	1.00	1.00
Howard Beach	0.97	1.21	1.11
Westchester	1.11	1.05	1.08
Fathers			
Riverhead	1.00	1.00	1.00
Howard Beach	0.98	1.28	1.19
Westchester	1.07	1.09	1.09
School children			
Riverhead	1.00	1.00	1.00
Howard Beach	1.17*	1.36*	1.27*
Westchester	1.09	1.34*	1.22*
Preschool children			
Riverhead	1.00	1.00	1.00
Howard Beach	0.99	0.85	0.89
Westchester	1.31	0.88	1.02

*$P < .01$

increases in respiratory illness,[20] but this factor was also controlled by the regression analysis. Occupational exposure was not thought to be important, since persons with potentially significant occupational exposure (4% of study individuals) were eliminated from the study population after the initial interview. There were differences between study communities on socioeconomic status as indexed by crowding; however, the regression analysis was adjusted for this factor, and indicated that it was important only among the two groups of children. An effort to control climate as an important factor prompted the selection of communities in the same geographic region. Annual mean rainfall did not differ among communities, but annual mean temperatures were one or two degrees lower in Riverhead than in the other study communities.[21]

Finally, although the results of this study are supportive of an air pollution effect, the possibility that there may be other significant urban factors cannot be ignored. Riverhead is farther from the center of the New York City metropolitan area than are the other areas, and is, consequently, the least urban of the study sectors. It is possible that lifestyle factors associated with less urban stress reduce the reported incidence of ARD. This study was not designed to evaluate this variable as a risk factor for ARD. Census data did show differences among the source populations from which the study groups were drawn.[22] It must be emphasized, however, that the study populations were selected groups and therefore not comparable to the census tract populations.

If community differences in air pollution levels were responsible for the observed higher rates of ARD in Howard Beach and Westchester, the relative excess attributed to air pollution appears to be almost as large among adults as among children.

Since the levels of air pollution exposure in Howard Beach and Westchester during the period of this study were probably below the U.S. primary air quality standards, it might be concluded that adverse health effects still occur in areas where air standards are no longer exceeded. The authors do not believe that this conclusion is warranted. First, as previously mentioned, the values of particulate air pollution reported in Table 1 underestimate by 10-30% the particulate pollution measured at the same place by the local New York City air monitoring network. Second, the readings of SO_2 obtained by the standard West-Gaeke method have recently been shown to be affected by temperature extremes and by the time interval between sample collection and analysis.[23] These other variables were not recorded during this study. In the opinion of the authors, the numerical data for air quality, given in Table 1, are useful in demonstrating that there were quantitative differences in ambient air quality between the three study areas. But shortcomings in the quality of these data prevent the attributing of observed disease excess to any absolute values for these pollutants. Furthermore, not all potentially important air pollutants were monitored, e.g., photochemical oxidants. Since all measured pollutants were shown to have higher levels in Howard Beach and Westchester than in Riverhead, it is not possible to attribute disease excess to any one of the pollutants exclusively; if

indeed the effect can be attributable to measured air pollutants. Eisenbud documented a dramatic improvement in air quality in New York City between 1965 and 1972,[24] as measured in terms of SO_2 and particulate matter concentrations. It is possible that, if ambient air pollution was responsible for the observed ARD excess in Howard Beach and Westchester, the documentation of this excess during the 1971-1972 school year might be evidence of a residual effect of the high pollution levels that existed from 1965-1968. The lack of evidence of a community effect among preschool children in this study supports the suggestion that current exposures were not hazardous.

The authors conclude that some of the observed excess ARD in Howard Beach and Westchester is attributable to the complex urban air pollution of New York City; other potential risk factors have been considered and were controlled in the analysis. It is recognized, however, that the conclusion about air pollution may be confounded by lifestyle differences between the highly urbanized Howard Beach and Westchester communities and the "small town" environment of a community on eastern Long Island. We also cannot attribute the observed ARD excess to the absolute levels of air pollution recorded during the study. We believe that a follow-up study of these populations is warranted, now that the air quality of the region has reached a relative plateau during the past 6 to 8 yr. Likewise, the technology now exists to monitor personal air pollution, and such data would be extremely useful in diminishing some of the bias due to misclassification of exposure status that invariably affects epidemiologic studies of community air pollution.

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*Pulmonary symptoms and pulmonary functional
tests among children in relation to the area of
residence*

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We have made an epidemiological study on a popula-
tion sample of 1331 Catalan children who live in two
different residential areas: 704 (322 girls and 382 boys)
from an industrial area in the greater Barcelona area,
with considerable heavy traffic and industrial pollu-
tion, and 627 (311 girls and 316 boys), from four rural
areas far from any focus of pollution.

All children were born between 1969 and 1971.
Anamnestic data (previous diagnosis of asthma, bron-
chitis, pneumonia and tuberculosis, number of colds,
symptoms with colds, familial smoking habits and
parental expectoration, were collected by means a self-
administered questionnaire (a modification of the
MRC questionnaire, filled in by the parents.

1123 answers to the questionnaire (84.4%), and 1042
results of the functional tests (78.3%) were obtained. A
statistically significant association between diagnosis of
airways disease (asthma or bronchitis) and residence in
urban area was observed. P<0.01. No association was
found between the number of colds and the residential
area, nor between dry cough accompanying colds and
residential area. The presence of productive cough and
wheeze with colds was significantly more frequent in
the urban area (P<0.01).

Parental smoking habits and other family members'
smoking habits were analysed. No difference in the
number of cigarettes smoked daily in each area was
observed, nor any association with the presence of
children's bronchial symptoms or with the history of
airways disease.

A strong association between mother's phlegm and
children's respiratory symptoms was observed

(P<0.001). No association between father's phlegm
and children's symptoms was found.

A significant difference in the mean value of FVC
and FEV1 between sexes was observed, therefore, we
analysed both sexes separately in the following
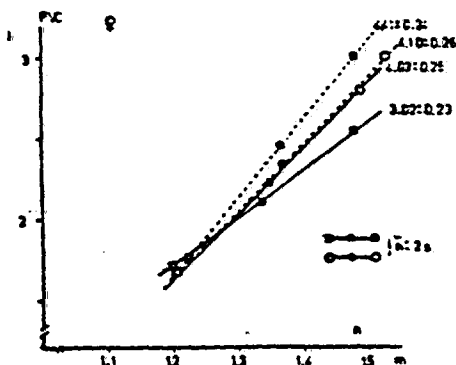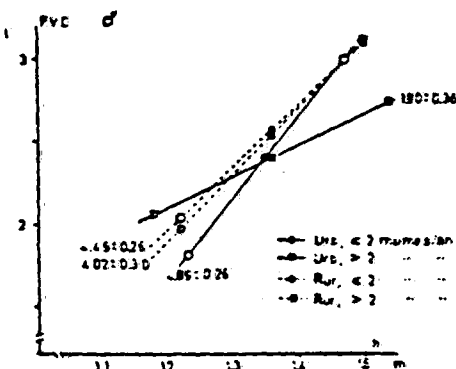
Correlation between FVC and height, according to
residential area and annual number of colds. Upper
graph refers to boys, lower graph refers to girls. Figures
refer to mean values ±2 s.d. of the slope of each
correlation.

statistical analysis: children living in the urban area showed a significant relative reduction of FVC and FEV₁ compared with children living in the rural area (P≤0.01 and P≤0.001). We also observed a difference in height: children living in the rural area were taller than children living in the urban area.

The analysis of differences between the regression slopes of FVC and FEV₁ on height showed a highly significant difference between the two areas. The value of the slope of the regression in the urban area was lower than the value of the slope in the rural area.

The same regression analysis was made concerning FVC and FEV₁ in relation to the other factors collected in the questionnaire. A systematic association was only found with the number of colds: children who lived in the urban area and had frequent colds showed a significant reduction in the regression slope (Fig. 1).

Discussion

Significant differences were found in the development of respiratory function in relation to height. Factors which seem to influence this relationship are residential area and the annual number of colds.

We did not find any difference when we compared the regression slopes of the FVC and FEV₁, thus we can state that the number of colds and residential area have direct influence on the FVC. This relative functional defect could be explained by a lower volume development, by a small airways obstruction or by a combination of both. Unfortunately, we did not measure slow vital capacity, which could have allowed us to discriminate the role of each one of these factors.

The fact which mostly determines differences between the two areas is industrial level. Therefore, air pollution might play a relevant role in determining a

different natural history of lung disease.

When symptoms with colds were analysed, a higher frequency of productive cough and wheeze among children living in industrial areas could be seen. However, the incidence of colds is the same in the two areas; when each group of children is analysed according to the annual incidence of colds, children living in the industrial area who get colds frequently, present a worse evolution of respiratory function tests in relation to their height.

A strong correlation between maternal productive cough and respiratory symptoms among children has been found. While maternal smoking habits have been suggested as a possible cause of this association, our study did not yield an association between maternal smoking habits and children's respiratory symptoms. We must take into account that these data were obtained by means of a self-administered questionnaire. Therefore, as in most cases the mother filled in questionnaires, the association we found between maternal and children's productive cough could be due to the mothers' different interpretation of what is productive cough or phlegm.

Conclusions

In our study, residence in an industrial area and the association of this with the frequency of colds are associated with impairment of the development of pulmonary function. We have also found an association between maternal productive cough and children's bronchial symptoms.

The contribution of these factors to the development of a chronic obstructive lung disease in adult life must be evaluated by means of cohort studies begun in childhood.

Could relationship between respiratory symptoms and lung function exist?

Janusz Haluszka. Institute for Mother and Child. Rabka Branch. Poland

Q.1. What is the physiological meaning of results of respiratory function tests and of answers to symptom questionnaires?

Most of the so-called lung function tests widely used in epidemiology, are in fact not measuring any function but simply reflecting changes in the physical

properties of the lungs, which may in turn be influenced by other extra-pulmonary organs and by properties of the thoracic cage.

Respiratory symptoms recorded as subjective answers to standard questions have an even more complicated and ill-defined physiological meaning. Each of the symptoms can have multiple causations, most of which have not been defined. In the field of epidemiology it is particularly easy to allow other factors to influence the physiological meaning of answers given in questionnaires: for example the subjectivity of symptom evaluation, incorrect interpretation of a

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Dodge, Russell "The Effects of Indoor Pollution on Arizona Children" Archives of Environmental Health 37(3): 151-155, 1982.

ABSTRACT. The respiratory health of a large group of Arizona school children who have been exposed to indoor pollutants-tobacco smoke and home cooking fumes-is reported. A significant relationship was found between parental smoking and symptoms of cough, wheeze, and sputum production. Also, children in homes where gas cooking fuel was used had higher rates of cough than children in homes where electricity was used. No differences in pulmonary function or yearly lung growth rates occurred among subjects grouped by exposure to tobacco smoke or cooking fuel. Thus, parental smoking and home cooking fuel affected cross-sectional respiratory symptom rates in a large group of Arizona school children. Study of pulmonary function, however, revealed no lung function or lung growth effects during 4 yr of study.

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The Effects of Indoor Pollution
on Arizona Children

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ABSTRACT. The respiratory health of a large group of Arizona school children who have been exposed to indoor pollutants—tobacco smoke and home cooking fumes—is reported. A significant relationship was found between parental smoking and symptoms of cough, wheeze, and sputum production. Also, children in homes where gas cooking fuel was used had higher rates of cough than children in homes where electricity was used. No differences in pulmonary function or yearly lung growth rates occurred among subjects grouped by exposure to tobacco smoke or cooking fuel. Thus parental smoking and home cooking fuel affected cross-sectional respiratory symptom rates in a large group of Arizona school children. Study of pulmonary function, however, revealed no lung function or lung growth effects during 4 yr of study.

INDOOR AIR POLLUTION has been reported to adversely affect human health. While various occupational lung diseases have long been recognized as secondary to indoor pollution, more recent reports have concluded that the general population is also at risk from exposure to indoor pollution.[1-3, 6, 8] Among the forms of indoor pollution which may affect humans are tobacco smoke[2] and cooking fumes.[3] Children, because they are usually non-smokers, have been studied most frequently. Children of smoking parents have been observed to have more respiratory symptoms and lower lung function than children of nonsmokers.[4, 5] Similarly, children living in homes where gas is used as the cooking fuel have been reported to have more respiratory problems than other children.[6]

The results of studies of indoor pollution, however, have not been consistent. Some investigators have not found that parental smoking or home cooking fuel are important determinants of childrens' respiratory health.[7, 8] At present, these disparate findings are unexplained, but population or methodological differences in studies may be responsible. For example, children living in milder climates may be exposed to lower levels of indoor pollution than children in colder climates. Also, studies to date have been cross-sectional in nature, perhaps producing more variable results than longitudinal studies would.

The author, therefore, chose to conduct a longitudinal study of Arizona children who were exposed to indoor pollutants, findings of which are reported herein.

METHODS AND MATERIALS

The subjects of this study lived in small communities in Arizona: Morenci, San Manuel, and Kingman. Morenci and San Manuel have large copper smelters at the edge of town, but Kingman has no such pollution source. A comparison of respiratory health of the children grouped by exposure to smelter smoke revealed no differences, except in the prevalence of cough.[9] The communities had similar populations (range 4,000 to 7,312) and elevations (range 3,300 to 4,000 ft). The most important demographic difference among the towns was the percent of the subjects who were Mexican-Americans. Only 5% of the Kingman subjects were Mexican-American, whereas 40% of the San Manuel subjects and 57% of Morenci subjects were Mexican-American. Students, and parents of students, in the third or fourth grade in all

schools of Morenci and in one school each in San Manuel and Kingman were contacted. The schools in San Manuel and Kingman were selected because of relatively low out-migation rates. In 1978, 379 students were enrolled at the above-mentioned schools.

In 1979, the students whose parents had declined to participate in 1978, and a new cohort of third graders in the same schools, were contacted. By the end of 1979, 676 students from these schools were participating in the study. The participation rate at the end of 1979 was 76.3%, i.e., 676 of the 884 students contacted in 1978 or 1979 were enrolled. According to the percent of students with Spanish surnames on school enrollment lists, study participation was roughly equal in the two ethnic groups.

Enrolled subjects' parents completed questionnaires on enrollment in 1978 or 1979. The questionnaires contained sections concerning the subjects, their mothers, and their fathers. The majority (62.67%) of the parents completed follow-up questionnaires in 1980.

A few subjects completed the follow-up questionnaire only. The first questionnaire contained questions selected from the questionnaire of the Tucson Epidemiologic Study of Obstructive Lung Disease.[10] The follow-up version contained the same questions plus some new questions about home cooking and migration. Based on the parents' responses to specific questions on either the 1978–79 questionnaire or the follow-up one, prevalence rates for various respiratory problems were established. For example, if the response was YES to the question "Does he or she ever have wheezing or whistling in the chest?" the subject under consideration was listed among those with "wheeze."

Another brief questionnaire was administered to the students who were in the sixth grade in 1980. Questions about cigarette smoking and the symptoms of cough and wheeze were asked. No students reported daily cigarette smoking.

Spirometry was performed on each child with either of two rolling dry-seal CPI spirometers. These two instruments were calibrated before each set of tests and were used all 4 yr with approximately one-half of the children using each one each year. No efforts were made to select which children blew into which machine. A nurse-interviewer with extensive experience in pulmonary function testing and the author conducted the testing. Each child was seated, instructed on performing a maximum expiratory maneuver, and given nose clips. Each child then completed at least three maneuvers. Further efforts were obtained from children who did not produce a second best forced vital capacity (FVC) within 5% of their best FVC. The single best forced expiratory volume in one second ($FEV_{1.0}$) was used in the analyses. These values were corrected for barometric pressure and temperature.

Of the 676 children who participated in the study, and who had the sections of the questionnaires completed about their health, 628 had all additional questions completed which asked about their parents' health (Table 1). The discrepancy primarily reflects the number of single-parent families in which questionnaires for a father were not completed. Also, 419 children's parents completed the 1980 questionnaire, which asked about home cooking fuel (Table 2). Of the 676 subjects, 558 had both a satisfactory pulmonary function test result and questionnaire responses to ques-

Table 1.—Prevalence of Various Respiratory Problems in Subjects Grouped by Parental Smoking

	Parent Reports % with					Child Reports % with		
	N	Asthma	Wheeze	Sputum	Cough	N	Wheeze	Cough
Both parents smoke	146	7.6	41.1†	12.3†	27.4*	28	21.4	14.3
Anglo-whites	116	7.8	42.2	12.1	24.1			
Mexican-American	30	6.7	36.7	13.3	40.0			
Adjusted rate‡	146	7.5	40.0†	12.0†	27.8*			
One parent smokes	185	5.5	28.0†	11.4†	23.2*	34	11.8	5.9
Anglo-whites	102	7.9	32.0	10.8	25.5			
Mexican-American	83	2.5	22.9	12.0	20.5			
Adjusted rate‡	185	5.2	27.9†	10.9†	23.0*			
Neither parent smokes	297	4.1	27.9†	6.7†	14.1*	62	8.1	6.5
Anglo-whites	168	5.4	31.0	6.5	13.7			
Mexican-American	129	2.3	24.0	7.0	14.7			
Adjusted rate‡	297	4.1	27.6†	6.4†	14.6*			

*The rates of cough are significantly different among comparable subjects ranked by parental smoking ($P < .01$ by trend chi square).
†The rates of these symptoms are different among comparable subjects ranked by parental smoking ($P < .05$ by trend chi square).
‡Rate adjusted for differences in rates of parental smokers among areas of study.

tions about parental smoking. The results of the testing of these subjects are displayed in Figure 1. A cohort of 120 8-yr-olds, 163 9-yr-olds, and 87 10-yr-olds produced most of the results. These subjects all had at least three annual tests during the 4 yr of the study. Thus, among the test results displayed by age at testing in Table 1, 120/171, 277/365, 371/443, 307/356, and 192/209 of the tests (82.1%) were produced by the cohort with at least three annual tests. Other results are for subjects who had only one or two annual tests.

Of the 676 subjects, 427 had at least one test result and questionnaire response to home cooking and were included in Figure 2. A cohort of 107 8-yr-olds, 134 9-yr-olds, and 79 10-yr-olds produced most of the results in Figure 2.

In Table 3, only the 472 subjects who had (1) a minimum of two consecutive annual tests and (2) appropriate questionnaire responses to parental smoking and in the lower portion of the Table, the 407 subjects who had (1) a minimum of two consecutive annual tests and (2) appropriate questionnaire responses to home cooking are included. A cohort of 119 8-yr-olds, 162 9-yr-olds, and 87 10-yr-olds produced 89.5% of the data for subjects grouped by parental smoking by undergoing annual testing at least three times. A similar, but slightly smaller cohort produced 92% of the data for the subjects grouped by home cooking.

Chi square, trend chi square, and analysis of variance are the statistical methods used in this report.[11]

RESULTS

Table 1 shows the rates of various respiratory symptoms and asthma in the subjects both overall and when grouped by parental smoking and ethnic background. A significant relationship between parental smoking and each of sputum production and cough occurred (less so by trend chi square). Because symptoms occurred more frequently in children from certain areas,[9] the rate of symptoms are also shown with an adjustment for the slight differences in the rates of parental smoking among the areas where children lived. Again, a significant trend occurred.

In an attempt to avoid the possible bias of smoking parents more readily reporting symptoms in their children than nonsmoking parents, a subset of older subjects were asked about cough and wheeze, the results of which are shown in Table 1. While the differences did not reach statistical significance, children of smoking parents reported more symptoms than children of nonsmoking parents.

Table 2 shows the rates of symptoms and asthma among the subjects grouped by home cooking fuel. The rate of cough was higher ($P < .05$ by chi square) in children who lived in homes where gas was used as a cooking fuel. In the Table, an adjustment for differences in home cooking fuel in the different areas of residence was made, as in the analysis of the effects of parental smoking, with little change in the rates.

The results of pulmonary function testing in the children are in Figures 1 and 2 and Table 3. The figures display $FEV_{1.0}$ vs. age at time of testing. Table 3 shows lung growth in the subjects who had at least two annual testings 1 yr apart. Lung growth was calculated by subtracting

Fig. 1. Lung Function in Subjects Grouped by Parental Smoking.

Age at Testing	8	9	10	11	12
No. of Subjects in Each Age Group	171	365	443	355	209

▲ No Parent Smokes
○ One Parent Smokes
● Two Parents Smoke

Fig. 2. Lung Function of Subjects Grouped by Home Cooking Fuel.

Age at Testing	8	9	10	11	12
No. of Subjects in Each Age Group	129	282	354	279	162

● Gas
■ Electric

$FEV_{1.0}/Height^3$ for 1 yr from $FEV_{1.0}/Height^3$ for the year before. The formula is:

$$Lung\ Growth = FEV_{1.0_{age+1}} / (Height_{age+1})^3$$
$$- FEV_{1.0_{age}} / (Height_{age})^3$$

Parental smoking and home cooking fuel did not consistently affect yearly lung function or lung growth.

DISCUSSION

The present report shows that children of smoking parents and children living in homes with gas cooking fuel had more respiratory symptoms

Table 2.—Prevalence of Various Respiratory Problems in Subjects Grouped by Type of Home Cooking Fuel Used

	N	Asthma	Wheeze	Sputum	Cough
Subjects with gas as home cooking fuel	340	4.7	30.6	10.3	20.3*
Adjusted rate†		4.4	31.1	10.1	19.7*
Subjects with electricity as home cooking fuel	79	3.8	29.1	3.8	8.9
Adjusted rate†		3.1	26.7	4.7	10.0

*Rate of cough is significantly higher in subjects with gas home cooking fuel ($P < .05$ by chi square).
†Rate adjusted for differences in rates of gas home cooking fuel among areas of study.

Despite the higher rate of symptoms, however, these subjects had no impaired lung function or lung growth during the 4-yr study. Because of the population studied and the methods used, these result have limited application.

The subjects studied do not represent the general population well. Roughly two-thirds of the children lived in Arizona smelter communities. The author has previously described that the smelter town children, who have been exposed to relatively high levels of sulfur dioxide have a higher prevalence of cough than other children, but comparisons of other symptoms and lung function revealed no differences.[9] Still, smelter town children may be particularly hardy and resistant to the effects of tobacco smoke or gas cooking fumes. When the non-smelter town children were analyzed separately, the results did not differ qualitatively from those when the entire cohort was analyzed. Socioeconomical status differed when the children from different areas were compared, but the status did not affect symptom rates or lung function. Thus, the non-smelter town children and smelter town children appeared to be similarly affected by the variables of parental smoking and home cooking fuel.

The subjects were not randomly selected members of the communities. Approximately one-fourth of the students eligible did not participate, and about 35% of those who did participate contributed only one or two acceptable yearly lung function tests. The subjects who participated for 3-4 yr, then, may not be representative of the general population.

The methods used also limit the application of the study results. No measurements of indoor pollutants were made, therefore, the relation of questionnaire information to actual exposures is unknown. In addition, the questionnaires only asked about parental smoking. While the households with two smoking parents averaged 5.2 persons per household, the same number as households with non-smoking parents, other smokers undetected by the questionnaires may have been present or parents who smoked but did not live with the subject may have been absent. Such persons would have blurred the groupings used in the present analyses.

Despite the above limitations, the study provides evidence that parental smoking and home cooking do not produce serious respiratory problems in Arizona children. I found, as have others,[4] that children of smoking parents have more respiratory symptoms than other children. To avoid parental reporting bias,[12] all the 1980 sixth graders were asked about respiratory symptoms. While the differences did not reach statistical significance, they again suggested the children of smokers had more symptoms.

Table 3.—Lung Growth of Subjects Expressed as $FEV_{3.0_{age+1}}/(Height_{age+1})^3 - FEV_{3.0_{age}}/(Height_{age})^3$

	N	Age 8-9 yr	N	Age 9-10 yr	N	Age 10-11 yr	N	Age 11-12 yr
Both parents smoke	22	61.84*	62	63.40	73	65.28	47	66.40
One parent smokes	41	68.54	87	65.21	94	64.50	54	68.07
Neither parent smokes	75	64.94	156	65.34	145	64.13	90	67.75
Gas home cooking	94	65.68	204	65.13	211	64.19	132	67.71
Electric home cooking	29	65.80	49	65.31	46	64.93	23	66.16

*The lung growth is significantly different among the subjects 8-9 yr of age ($P < .05$ by ANOVA).

Also, in agreement with other investigators,[6] I found that children who lived in homes with gas as the cooking fuel coughed more frequently than the other subjects.

The pulmonary function testing showed that neither parental smoking nor gas home cooking fuel adversely affected lung function or yearly lung growth. Tager et al.[5] reported decreased pulmonary function in children of smokers. Others have not found such differences.[7] Similarly, varied results of the effects of gas cooking have been reported.[6,7] To ensure that differences in height did not obscure differences in lung function among the subjects, I also calculated lung growth for each subject who had two or more tests. These results showed that with height cubed taken into consideration, lung growth was not affected by parental smoking or home cooking. Also, when initial lung function was taken into account, by calculating lung growth over the entire period of the study in subjects grouped by initial $FEV_{1.0}$, no differences in the various parental smoking or home cooking groups were found. The results of the present study are good evidence that these factors do not affect the lung function of children living in the southwestern United States. Indoor monitoring, now in progress, may confirm the suspicion that particulate and nitrogen dioxide levels are much lower in the highly ventilated homes of this region than in colder climates.

In conclusion, while parental smoking and home cooking fuel can influence respiratory symptom rates among Arizona children, these variables do not adversely affect lung function or growth.

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Ferris, B.G., Dockery, D.W., Ware, J.H., Speizer, F.E., Spiro, R.
"The Six-City Study: Examples of Problems in Analysis of the Data"
Environmental Health Perspectives 52: 115-123, 1983.

ABSTRACT. This paper presents some of the results from cross-
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Similar examples are presented for illness rates for four
respiratory diseases: asthma, bronchitis, illness before age 2
and illness last winter. These examples of cross-sectional analyses
emphasize the ambiguities of studies of possible health effects of
air pollution exposures close to the present ambient air quality
standards.

The Six-City Study: Examples of Problems in Analysis of the Data

by B. G. Ferris, Jr., * D. W. Dockery, * J. H. Ware,† F. E. Speizer‡ and R. Spiro III*

This paper presents some of the results from cross-sectional analyses and studies during air pollution alerts obtained as a part of the Six-City Study, a longitudinal study of the respiratory effects of air pollution. These analyses illustrate some of the limitations and uncertainties of epidemiologic studies. For example, an earlier report noted increased respiratory illness rates for children living in homes where gas was used for cooking. A later analysis did not confirm this. Reasons for this are explored by using different criteria and variables to be controlled for. The results illustrate that the strength of the association between cooking fuel and illness was sensitive to the definitions of the variables and the number of subjects and city cohorts. Similar examples are presented for illness rates for four respiratory diseases: asthma, bronchitis, illness before age 2 and illness last winter. These examples of cross-sectional analyses emphasize the ambiguities of studies of possible health effects of air pollution exposures close to the present ambient air quality standards.

Introduction

This paper describes some results from cross-sectional analyses and studies during air pollution alerts performed as part of the Six-City Study, a longitudinal study of the respiratory health effects of air pollution. These analyses illustrate some of the limitations and uncertainties of epidemiologic studies. We begin with a brief outline of the study design.

The Six-City Study was designed to test the adequacy of the present federal standards for SO_2 and particulates, to develop data on the effects of small particles, to assess the representativeness of a central station as an index of exposure and to assess the effect of the home environment in modifying exposure as indicated by outdoor levels. We planned to study primarily chronic effects but it was soon apparent that short-term fluctuations in air pollutants, particularly in Steubenville, offered the chance to study possible acute effects.

The six cities studied were selected on the basis of their historical levels of pollutants to include clean cities, cities close to the present standards for SO_2 and particulates, and cities above the standards. The six cities selected are listed in Table 1. The time of year that the city was visited also is indicated.

Methods

Random samples of adults were selected for study in each city from various census lists that were available. We attempted to obtain 1500 adults per city. The children selected were first and second graders. Additional cohorts of chil-

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Table 1. Cities studied by pollution category and time of year.

City	Season	Pollution category
Portage, WI	Fall	Clean
Topeka, KA	Spring	
Watertown, MA	Fall	Somewhat below standard
Kingston-Harriman, TN	Spring	
St. Louis, MO	Fall	Above standard
Steubenville, OH	Spring	

dren were added in subsequent years from the new first grade and new additions to the grades under study until about 2000 children were enrolled in each city. The adults were studied every third year and the children every year. Contact was maintained with the adult sample by mailing annual reports of the study. Respiratory health effects in both adults and children were assessed by means of a standard respiratory questionnaire and simple tests of pulmonary function. Smoking and occupational histories were obtained on the adults. Smoking habits were asked of the children when they reached the fourth grade or at age 9 years. Home characteristics such as air conditioning, heating and cooking fuels and number of smokers in the home also were tabulated.

Air monitoring was carried out in each city at a central site and at satellite sites in the community. Indoor and outdoor levels of a variety of pollutants were measured at each satellite site. Personal sampling was carried out to assess whether our modeling of estimated exposure has been reasonable. The pollutants and sampling methods are summarized in Table 2. The continuous methods are calibrated by our own team as well as by the Environmental Protection Agency. EPA also makes quality checks on our analytic procedures at regular intervals. The collection of bubbler samples is organized to coincide with the regular EPA sampling schedule. A more detailed description of the study is given in a previous report (1).

Results

Let us now look at some of the data and analyses and examine some of the problems we see in these analyses.

Steubenville Alert Study

In an attempt to quantify the impact of acute air pollution exposures on pulmonary function, we measured the pulmonary function of approximately 200 school children in Steubenville, Ohio, before, during and following periods of high air pollution concentrations.

In the fall of 1978, baseline measurements of pulmonary function were obtained on third and fourth graders between October 16 and 23. On November 5, total suspended particulate (TSP) concentrations reached 422 μg/m³ at the offices of the Northern Ohio Valley Air Authority (NOVAA) in Steubenville (Fig. 1). Because of previously determined criteria involving precipitation forecasting and levels of air pollution, NOVAA declared an "alert." The 24-hr mean sulfur dioxide (SO_2) concentration was 211 μg/m³ on November 5 and climbed to 272 μg/m³ on November 6. The National Primary Ambient Air Quality Standard for 24-hr concentrations of TSP is 260 μg/m³ and for SO_2 is 365 μg/m³. The children were retested on November 6 and 7 and weekly for the next 3 weeks. Each child's pulmonary
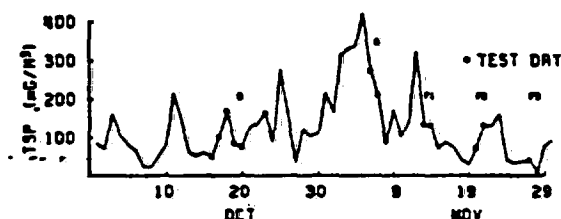
FIGURE 1. Fall 1978 alert. TSP concentrations measured at the NOVAA offices in Stuebenville, OH. Spirometric testing days are indicated by squares. (B) = baseline, (A) = alert, (F1) = follow-up 1, (F2) = follow-up 2 and (F3) = follow-up 3.

Table 2.

	Pollutant	Period	Sampler	Additional analysis
Central site	SO_2, NO_2, O_3	1 hr	Continuous	
	SO_2, NO_2	24 hr	Bubbler	
	TSP	24 hr	Hi-volume	Sulfates
	Fine and coarse particles[a]	24 hr	Dichotomous	X-Ray fluorescence
	Mass respirable particles[b]	24 hr	Cyclone	Neutron activation Sulfates
Satellite (indoor and outdoor)	SO_2, NO_2	24 hr	Bubbler	
	Mass respirable particles[b]	24 hr	Cyclone	Neutron activation Sulfates
Personal	Mass respirable particles[b]	24 hr	Cyclone	Sulfates
	NO_2	7 day	Palmes tubes	

[a]"Fine" defined as < 2.5 μm aerodynamic diameter; "coarse" defined as 2.5-15 μm aerodynamic diameter.
[b]50% cut at 3.5 μm aerodynamic diameter.

function measurements during the alert (A) and at follow-up tests (F1, F2, F3) were compared to their own values during the baseline tests (B). Thus, sex and race are not considered in the analysis.

For those children seen on all five visits, $FEV_{1.0}$ averaged 12 mL lower at the alert and follow-up visits compared to the baseline values (Fig. 2). The mean $FEV_{1.0}$ at the baseline measurement of these children was 1.686 L. At the first follow-up visit (F1), mean decline in $FEV_{1.0}$ was 11 mL; in the second follow-up it was 15 mL; and in the third follow-up it was only 5 mL. As suggested by the standard errors about the mean, none of the declines reached a statistically significant difference from zero at the 0.05 level. The trend in the differences is consistent with a decline in the $FEV_{1.0}$ following the air pollution alert which may last several weeks. Other factors might have prevailed. We have examined the effect of levels of pollution on the day of the measurement and have explored the possibility that a few children could be driving the overall effect seen. We have also attempted to assess the effects of boredom of the children or the technicians.

If we subtract from each $FEV_{1.0}$ measurement the expected value for that child based upon a prediction formula using sex, race and height, we can correlate the residual $FEV_{1.0}$ values with the daily pollution concentrations for the 24 hr ending at 8 A.M. of the morning of the pulmonary function testing. This analysis is sensitive to a very short-term effect, with recovery within 24

hr. As seen in Figure 3, there is little correlation between mean residual $FEV_{1.0}$ and TSP concentrations that day for this study. The correlations with the other pollutants, SO_2 and NO_2, were not as high as that for TSP.

The study was repeated in the fall of 1979. Initially, the intent was to examine the effect of repeated weekly measurements of pulmonary function without an air pollution episode. Base-line measurements were made in October. On November 16, a "sham" alert was declared, and the children were restudied.

On November 20, TSP concentrations reached 271 $\mu g/m^3$ and SO_2 concentrations reached 439 $\mu g/m^3$. Both values exceeded the 24-hr standard. An alert was called. Children in school on November 21, which was the day before the start of Thanks-giving vacation, were retested. All the children were retested weekly for the following 3 weeks. Differences in $FEV_{1.0}$ compared to baseline (Fig. 4) showed an increase on the sham alert day (S) and a decline following the actual alert. Although larger than the measured declines in 1978, the differences were not significantly different from zero at the 0.05 level for those children who were tested all six times. As in the 1978 alert, the $FEV_{1.0}$ residuals did not correlate well with the daily TSP, SO_2 or NO_2 concentrations.

The following spring, in 1980, these same children were tested again in a sham alert for five consecutive weeks. $FEV_{1.0}$ declined in a pattern very similar in shape and magnitude to that seen in the previous alert studies (Fig. 5). The air
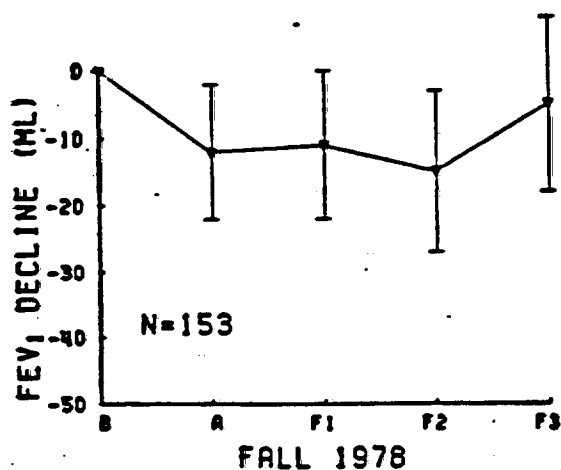
FIGURE 2. Mean difference in $FEV_{1.0}$ compared to baseline measurement for those children tested on all five visits in the fall 1978 alert study. Vertical bars denote one standard error above and below the mean.
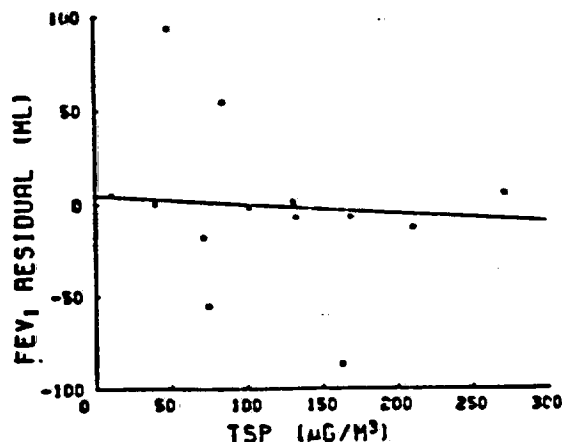
FIGURE 3. Mean residual $FEV_{1.0}$ for each testing day in the fall 1978 alert study plotted against mean TSP concentrations for the 24 hr ending at 8 A.M. for that day. The best-fit line, based on least squares weighted by the number of children tested each day, is also shown ($R = 0.15$).
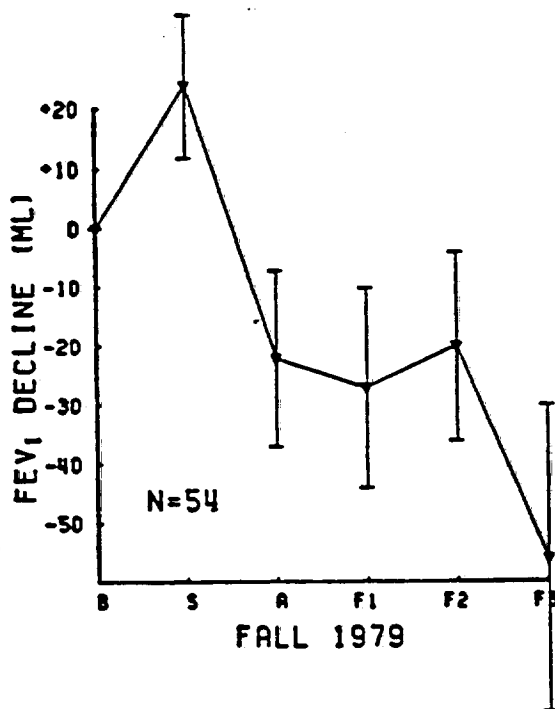
FIGURE 4. Mean difference in $FEV_{1.0}$ compared to baseline, with standard errors, for those children tested on all six visits during the fall 1979 alert study.

FIGURE 5. Mean difference in $FEV_{1.0}$ compared to baseline, with standard errors, for those children tested on all five visits during the spring 1980 sham alert.

pollution concentrations, as illustrated by the daily mean TSP level (Fig. 6), were relatively low. The maximum TSP was 220 µg/m³, and the maximum SO_2 was 169 µg/m³. This suggested that the observed declines might be a result of fatigue, or lack of interest by the children. On the other hand, there was a very high correlation between the mean residual $FEV_{1.0}$ for each day and the TSP concentration in the spring 1980 study (Fig. 7).

In a further attempt to understand the changes in pulmonary function which had been observed, these same children were tested again in the fall of 1980 for five consecutive weeks (Fig. 8). During this period, TSP had a maximum concentration of 159 µg/m³, and SO_2 a maximum concentration of 166 µg/m³. $FEV_{1.0}$ again showed declines similar to those seen following the air pollution alerts. The correlation of daily TSP with residual $FEV_{1.0}$ was fairly good ($R^2 = 0.204$).

Discussion

These four studies provide suggestive but inconclusive evidence concerning the relationship between short-term changes in air pollution con-

centration and the level of $FEV_{1.0}$. Taken together, these children exposed to sudden increases of TSP and SO_2 concentrations near or above the current 24-hr standards had declines of 1 to 2% in $FEV_{1.0}$. These changes are small relative to sampling variability and are marginally significant.

We also need to evaluate the medical significance of such changes in pulmonary function. That is, do they lead to a permanent effect? Initial cross-sectional comparisons of the levels of pulmonary function show that Steubenville children have values comparable to those in the other cities in spite of presumably having experienced similar high, or higher, levels of short-term TSP and SO_2 peaks in the past. To reduce the potentially confounding effects of other factors, we are following these children prospectively to compare lung function development in these children to that in similarly aged children from other cities in which no such short-term peak exposures have occurred.

Children's Illness Prevalence

The second set of analyses to be discussed describes associations between illness rates for children living in the six cities and potential risk factors such as passive smoking or the use of gas cooking fuel. The following points will be emphasized. First, the effects of environmental risk factors on respiratory disease rates are sensitive to what may be termed the 'style' of analysis adopted. That is, different results may be obtained depending on: (a) definitions of the risk factors; (b) the composition and selection of the sample analyzed; and (c) the set of additional
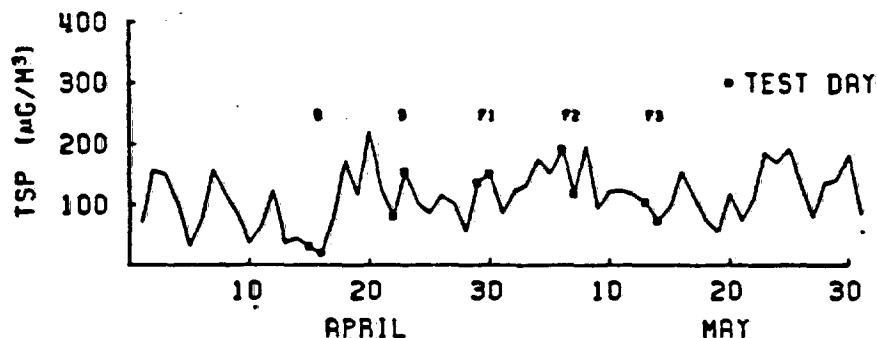
FIGURE 6. TSP concentrations for 24 hr measured in Steubenville during the spring 1980 sham alert with spirometric testing days indicated.
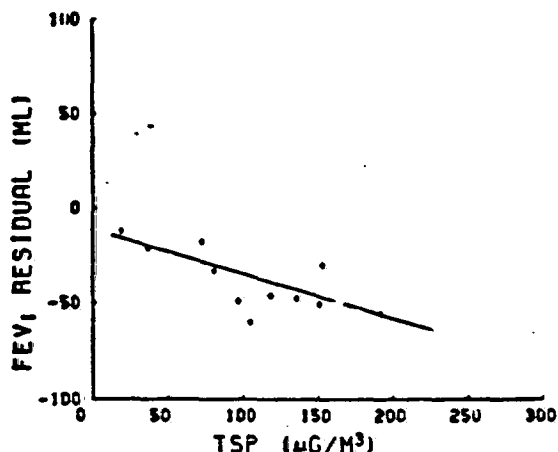
FIGURE 7. Mean residual $FEV_{1.0}$ for each testing day in the spring 1980 sham alert plotted against mean TSP concentrations for the 24 hr ending at 8 A.M. for that day.
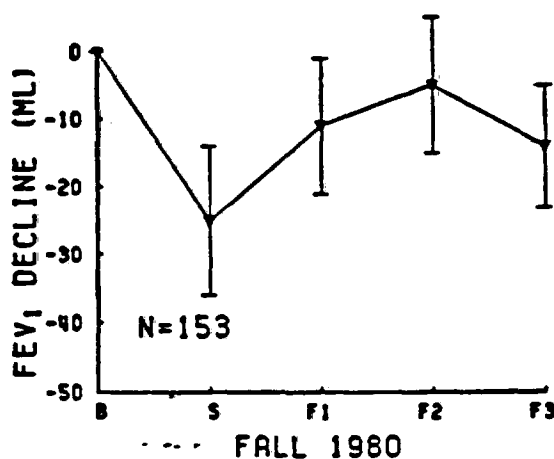
FIGURE 8. Mean difference in $FEV_{1.0}$ compared to baseline measurements and standard errors during the fall 1980 sham alert study.

variables included in the analysis. This sensitivity will be illustrated in the analyses of the prevalence of history of respiratory illness before age 2. Second, information will be presented on rates by city for four respiratory diseases: asthma, bronchitis, illness before age 2, and respiratory illness last year.

In a recent attempt to extend results reported earlier by our group (2) on the relationship between prevalence of respiratory illness before age 2 and cooking fuel, we repeated the analysis after including an additional four cohorts of children enrolled during 1978-1979. In this reanalysis, the association between illness before age 2 and cooking fuel was not statistically significant at the level of $p < 0.05$. This led to a closer comparison of the two analyses to determine why the result was not more closely replicated.

There was one obvious difference noted between the original and the more recent analysis. In the original analysis the data from 10 city-cohorts were pooled over sex. In the recent analysis, data from 14 city-cohorts (an additional 1493 children) were examined separately by sex. On closer examination, several other differences in variable definition were noted between the two analyses. In the first analysis, the cooking variable contrasted homes using gas only with those using electricity only. In the more recent analysis, the cooking variable contrasted homes using some gas with those using any other fuel. In the earlier analysis, the smoking variable indicated whether anyone in the home smoked. In the later analysis, this variable indicated only maternal smoking. Finally, socioeconomic status (SES) was defined differently in the two analyses. In the

first, it was based on both parents' education and occupation. In the second, it was based on a simple average of the parents' education.

Table 3 gives the strength of the association between illness before age 2 and cooking fuel in various analyses conducted to investigate the difference between the original result and the more recent analysis. Results are given for the pooled data and for boys and girls examined separately. For each analysis, the number of subjects is given, and the χ^2 test with one degree of freedom for association between cooking fuel and illness is presented. Finally, Table 3 presents the probability value for each of the analyses.

In analysis 1 in Table 3, reported earlier by us (2), the data from 5660 children in 10 city-cohorts were pooled over sex and analyzed. There was a significant relationship between illness and cooking fuel ($p = 0.01$). Children from homes with gas cooking had higher rates of illness before age 2 than did children from homes with electric cooking. When boys and girls were analyzed separately, the relationship between illness and cooking was significant for girls ($p = 0.02$), but not for boys ($p = 0.20$), though the direction of the association was the same in both groups.

Analysis 2 was our initial reanalysis with the four added cohorts, and newly defined variables for SES, cooking fuel, and household smoking. The association between cooking and illness before age 2 did not achieve statistical significance either for girls ($p = 0.12$) or for boys ($p = 0.48$). Because of this difference in the strength of the association, we believed it would be important to test individually how changes in the analysis affected the results.

Analysis 3 is comparable to analysis 1, except that SES and the cooking variable were defined as in analysis 2. That is, it contrasted homes using any gas cooking with homes using electricity or other cooking fuels. Formerly the cooking variable had contrasted homes using only gas with homes using only electricity. In addition the definition of SES used parental education only. These changes added 167 children to the data set compared to analysis 1. For the data pooled over sex, the relationship between illness and cooking was significant ($p = 0.04$). When the data were stratified by sex and analyzed separately, the relationship between illness and cooking was significant for girls ($p = 0.03$), but not for boys ($p = 0.49$).

In analysis 4 we added the four new cohorts. SES, smoking, and cooking were defined as in analysis 2. For the data pooled over sex, the relationship between illness and cooking was significant ($p = 0.04$). When the data were stratified by sex and analyzed separately, the relationship between illness and cooking was significant for girls ($p = 0.04$), but not for boys ($p = 0.44$).

To explain the discrepancy between analyses 2 and 4, we assessed the differences in the specific models used. In analysis 4, the effect of gas cooking was based on the original model used in analysis 1. It included an interaction term for city-cohort, smoking, and illness prevalence, but did not include an interaction term for SES and illness. In our new analysis (analysis 2) education and illness prevalence were significantly associated and there was no interaction between city-cohort, smoking, and illness. While the original model provided a satisfactory fit to the earlier data, it did not provide as adequate a fit to the enlarged data set as did a new model based on these data.

These results illustrate several problems in ex-

Table 3. Results of several analysis of the association between gas cooking and respiratory illness before age 2.

Analysis	N	χ^2	P
1 Original data, original model			
Pooled	5660	6.70	0.01
Boys	2936	1.59	0.20
Girls	2724	5.26	0.02
2 Enlarged data set, new modela			
Boys	3721	0.51	0.46
Girls	3433	2.44	0.12
3 Original data, SES, cooking fuel redefined			
Pooled	5827	4.16	0.04
Boys	3013	0.47	0.49
Girls	2814	4.61	0.03
4 Enlarged data set, SES, cooking fuel, smoking redefined			
Pooled	7153	4.13	0.04
Boys	3721	0.61	0.44
Girls	3432	4.06	0.04

aPooled analysis was not calculated.

ploratory analysis. The strength of the association between cooking fuel and illness was only modestly sensitive to the definitions of the variables (i.e., SES and cooking fuel), and to the number of subjects and city-cohorts. The initial analysis based on 10 cohorts was significant (analysis 1). The reanalysis with modified independent variables and additional cohorts was also significant (analysis 4). A lesser association was found (analysis 2) when parental education was included specifically in the analysis. This effect of model socioeconomic status (parameterized by parental education) is consistent with results reported from a similar study of children from western Pennsylvania (3).

The second example of the sensitivity of the data to the style of analysis concerns our examination of the illness rates in boys and girls.

This is shown in the evaluation of illness rates for four respiratory diseases: asthma, bronchitis, illness before age 2 and illness last year. The data were from 16 city cohorts (except for illness before age 2 which was based on 14 cohorts). Analyses were conducted separately for each sex, thus providing a total of eight analyses (four diseases × two sexes). The risk factors considered in each analysis were: city, cohort, maternal smoking, age, parental education, and cooking fuel. Log-linear analysis was used to study the relationships between each disease and the risk factors. Both step-up and step-down analyses were performed, and where the results diverged, the simpler model was chosen. Details of this analysis are presented elsewhere (4).

Figures 9-12 present the standardized illness rates by city separately for boys and girls. The rates for each disease and for each sex were adjusted by those risk factors shown to be significant ($p < 0.10$) in the analyses. For example, the rates were adjusted for maternal smoking in all analyses except those for asthma in both sexes and for illness last year for boys. The boys' bronchitis rate was adjusted by cooking fuel, parental education and maternal smoking. For bronchitis in girls, the rates were adjusted only by maternal smoking. For illness before age 2 in boys, the rates were adjusted for age as well as for maternal smoking. For illness before age 2 in girls, the rates were adjusted by parental education and maternal smoking. For illness last year in boys,
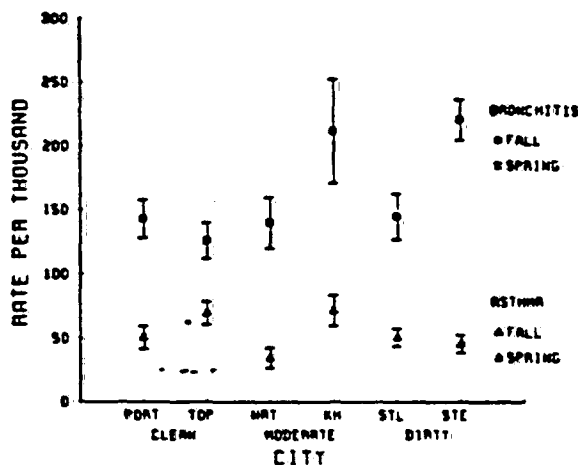
FIGURE 10. Illness rates for bronchitis and asthma for girls by city and season.
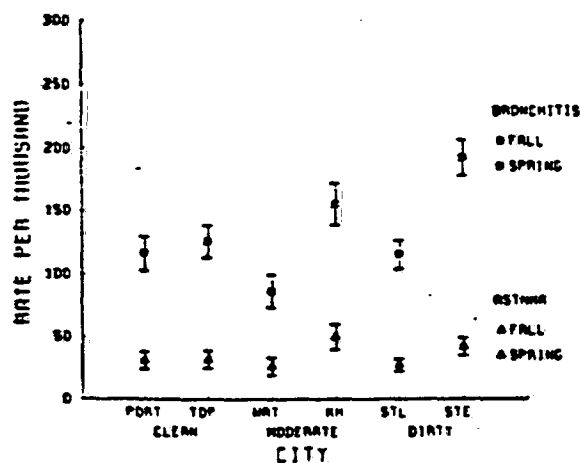
FIGURE 9. Illness rates for bronchitis and asthma for boys by city and season.
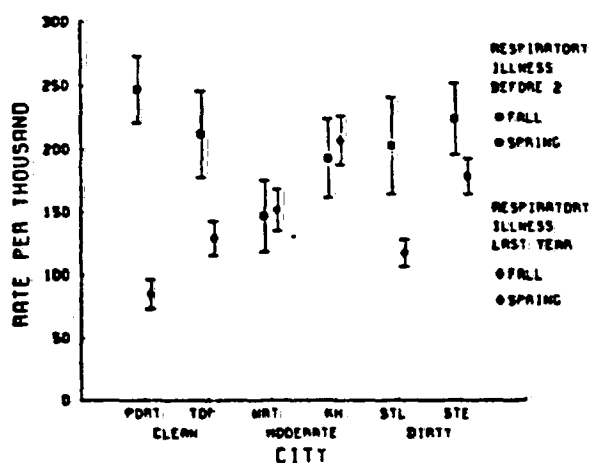
FIGURE 11. Illness rates for respiratory illness before age 2 and illness last year for boys by city and season.

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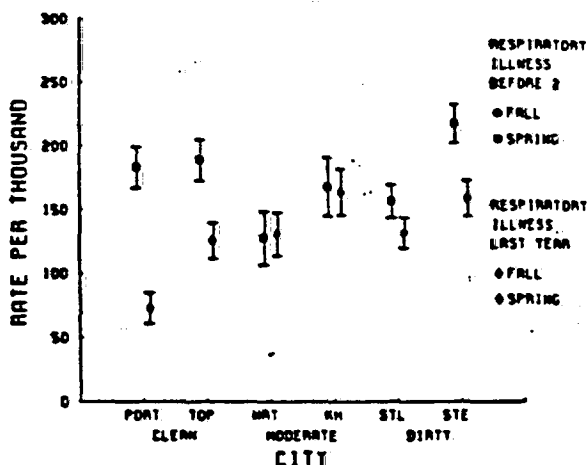
FIGURE 12. Illness rates for respiratory illness before age 2 and illness last year for girls by city and season.

the rates were adjusted by age. For illness last year in girls, the rates were adjusted by age and maternal smoking. The rates for asthma and bronchitis are shown in Figure 9 for boys and in Figure 10 for girls. The rates for illness last year and for illness before age 2 are shown in Figure 11 for boys and in Figure 12 for girls. Although differences between cities for reported history of illness before age 2 varied according to year of enrollment for boys, the rates were averaged over city to simplify the visual presentation.

For all diseases except asthma in girls, city was a significant factor. For asthma in boys, the city with the highest rate was Kingston-Harriman. For bronchitis, the cities with the highest rates for both boys and girls were Steubenville and Kingston-Harriman. For illness before age 2, the highest rate for boys was in Portage, while for girls it was in Steubenville. For illness last year, the highest rates for both sexes were in Kingston-Harriman. Generalizing across the seven analyses, Steubenville and Kingston-Harriman had the highest illness rates and Watertown the lowest.

Three cities (Portage, Watertown and St. Louis) were visited in the fall, and the others were visited during the spring. Because respiratory diseases are more common during the winter, and because a recent disease is more likely to be remembered than one a season or more earlier, it is revealing to examine the rates for the cities grouped by season. With this in mind, Figure 9 shows that bronchitis was higher for boys in the spring cities, and asthma shows little seasonal effect. Figure 10 shows that bronchitis was also

higher for girls in the spring cities. Figures 11 and 12 show that illness last year was higher in the spring cities. No trend was evident for illness before age 2. These data suggest that there is a bias in recall by the parents, with greater numbers of events reported for those reporting closest to the winter season just passed.

Maternal smoking was associated with history of bronchitis, illness before age 2, and illness last year in girls (p ranged from 0.04 to 0.06). Except for illness in the last year the same associations were found for maternal smoking and disease in boys (p ranged from 0.01 to 0.08). In all cases the illness rates were higher for children whose mothers smoked.

Cooking fuel was related only to boys' bronchitis. Boys in homes where gas was used for cooking had lower bronchitis rates than boys in homes using other cooking fuels. This is in contrast to the earlier reported finding concerning illness before age 2 in which children in homes with gas cooking had higher rates than children in homes with other cooking fuels.

Discussion

These examples of cross-sectional analyses illustrate potential pitfalls in analyzing studies of possible health effects of air pollution exposures close to the present ambient air quality standards. The analyses are sensitive to the sample composition and to the assumptions and variable definitions used. In addition, there are many confounding factors and the signal-to-noise ratio is small, so that even in relatively large studies, resolution may be difficult. It is useful to define variables and analysis plans prior to beginning the analysis to avoid subjectivity and data-dependent results. We hope that the prospective aspects of our study will help provide less ambiguous measures of the health significance of low level exposure to fossil fuel air pollutants.

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Schenker, M.B., Samet, J.M., Speizer, F.E. "Risk Factors for Childhood Respiratory Disease: The Effect of Host Factors and Home Environmental Exposures" American Review of Respiratory Disease 128: 1038-1043, 1983.

SUMMARY: Standardized respiratory disease questionnaires (ATS-DLD-78-C) were completed by the parents of 4,071 children 5 to 14 yr of age, and risk factors for respiratory symptoms were evaluated by logistic analysis.   Younger age, male sex, and lower socioeconomic status (SES) were independent risk factors for most respiratory symptoms and illnesses.   All respiratory outcomes were significantly more prevalent in children with a physician's diagnosis of asthma.   Asthma was more prevalent in male (4.5%) than in female (2.8%) children, and the greater prevalence of most respiratory symptoms in males did not persist in children with the same asthma status.   Children whose questionnaires were completed by their fathers were reported to have significantly fewer respiratory symptoms than children with mother-completed questionnaires.   We postulate that fathers underreport symptoms for their children.   A positive parental history of allergy or respiratory illness was an independent predictor of respiratory symptoms and illnesses in the children.   Chest illness before 2 yr of age and chest illness in the past year showed a significant positive linear trend with the number of parental smokers, and these effects of passive smoking were confirmed in the logistic analysis.   The use of gas cooking stoves, inversely associated with SES, was not an independent risk factor for any respiratory symptoms or illnesses.

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Risk Factors for Childhood Respiratory Disease

The Effect of Host Factors and Home Environmental Exposures[1-3]

M. B. SCHENKER,[4] J. M. SAMET,[5] and F. E. SPEIZER

Introduction

Since the 1960s, a few large population-based studies have been performed in the United States and other countries to examine the epidemiologic aspects of childhood respiratory disease (1-6). These investigations have often been designed to assess the effects of specific environmental exposures such as ambient air pollution (1, 5). In this regard, children as study subjects have several advantages over adults. They may be more susceptible to environmental pollutants than adults, and the outcome measures of interest are not affected by cigarette smoking and occupation. Children can also be readily examined in large numbers through their schools. The hypothesis that childhood factors may influence the development of chronic respiratory disease has provided additional impetus for investigations of children (7).

Barriers to the performance of such studies have included the lack of a standardized questionnaire and the difficulty of obtaining valid histories from children or their parents. In 1978, a standardized respiratory questionnaire — the American Thoracic Society, Division of Lung Diseases Questionnaire (ATS-DLD-78-C) for children — became available as a result of the Epidemiology Standardization Project of the American Thoracic Society (8). This type of survey instrument should facilitate study of the natural history of respiratory illness in children and evaluation of the effects of environmental exposures. The use of a standardized questionnaire will also allow comparison of results among different study populations.

This report is based on data from a study of air pollution health effects in the Chestnut Ridge region of Pennsylvania (9). One component of the study was a respiratory prevalence survey of 4,071 first through sixth grade children. The ATS-DLD-78-C questionnaire was completed by parents, and the children performed spirometry in the school. This report provides results from the use of this new questionnaire in a large population of children. We have used the questionnaire responses to describe the prevalences of respiratory symptoms and illnesses. Additionally, using a multivariate technique, we have evaluated the effects on respiratory symptom prevalences of host factors, environmental exposures, and potential sources of reporting bias.

Methods

Study Area

The study area is an approximately 700 square kilometer section of the Chestnut Ridge region, a geographic feature in western Pennsylvania that exceeds the study boundaries. The area is 150 kilometers east of Pittsburgh and consists of the lower half of Indiana County and parts of Armstrong and Westmoreland counties. The region is predominantly rural, and there are numerous underground coal mines and 4 large coal-fired electricity generating plants within the area.

Study Population

All public school districts within the study area agreed to participate in the study. Fourteen schools were selected from the public school districts to provide even geographic and age coverage of children in the area. The schools were grouped into northern, middle, and southern thirds of the study area, which approximated low, medium, and high air pollution regions, respectively. One or two schools were then selected at random from each geographic area for

SUMMARY Standardized respiratory disease questionnaires (ATS-DLD-78-C) were completed by the parents of 4,071 children 5 to 14 yr of age, and risk factors for respiratory symptoms were evaluated by logistic analysis. Younger age, male sex, and lower socioeconomic status (SES) were independent risk factors for most respiratory symptoms and illnesses. All respiratory outcomes were significantly more prevalent in children with a physician's diagnosis of asthma. Asthma was more prevalent in male (4.5%) than in female (2.8%) children, and the greater prevalence of most respiratory symptoms in males did not persist in children with the same asthma status. Children whose questionnaires were completed by their fathers were reported to have significantly fewer respiratory symptoms than children with mother-completed questionnaires. We postulate that fathers underreport symptoms for their children. A positive parental history of allergy or respiratory illness was an independent predictor of respiratory symptoms and illnesses in the children. Chest illness before 2 yr of age and chest illness in the past year showed a significant positive association with the number of parental smokers, and these effects of parental smoking were confirmed in the logistic analysis. The use of gas cooking stoves, and associated with SES, was not an independent risk factor for any respiratory symptoms or illnesses.

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testing in each third of the testing period. All testing was completed between February and May 1979.

Questionnaire Technique

The ATS-DLD-78-C children's questionnaire (8) and a consent form were sent to the parents of all children in Grades 1 through 6 in the target schools. Each child with a completed questionnaire and consent form performed spirometry at school in a standard manner. The questionnaire includes questions on demographic data, household environmental exposures, respiratory symptoms and illnesses, allergies, and parents' history. The parental history includes questions on education, occupation, smoking, and respiratory illnesses for the mother and father.

An interviewer-administered questionnaire on smoking habits was completed at school by each child in Grades 4 through 6. The interview was conducted away from teachers and other children. Cigarette smoking by children was defined as "having ever smoked 5 or more cigarettes and currently smoking."

The major respiratory symptoms were considered present when positive responses were given to the following questions:

Chronic cough: "Does he/she cough on most days (4 or more days/wk) for as much as 3 months of the year?"

Chronic phlegm: "Does this child seem congested or bring up phlegm, sputum or mucus from his/her chest on most days (4 or more days/wk) for as much as 3 months a year?"

Persistent wheeze: Positive response to A and B and/or to C of the following series of questions: "Does this child's chest ever sound wheezy or whistling: A. When he/she has a cold? B. Occasionally apart from colds? C. Most days or nights?"

We considered the respiratory disease history of either parent to be positive if an affirmative response was given to either of the questions: "Has a doctor ever said he/she had bronchitis? emphysema?" A positive parent's allergic history was defined as a positive response to doctor-diagnosed asthma or hay fever in either parent.

Data Analysis

The use of a parent-completed questionnaire resulted in a varying number of missing responses. For the symptom and illness questions, the range of missing responses was 0.4 to 4.8%. More information was missing for items related to the parents' illness history: an average of 3.6% for mothers and 10.2% for fathers.

A socioeconomic status scale (SES) was derived from the parents' occupation and education. Education was ranked by number of years of school completed and occupation by Census Bureau allocation categories (10). The ranks were then converted to percentiles, and a percentile based score was assigned for specific educational and

occupational groupings. The higher of each parent's education or occupation scores was used as the SES value for that parent. For the household, the higher of the SES scores of the parents was used. The household scores were then ranked and divided into quintiles to provide SES strata V (lowest) through I (highest).

Initial analyses were done with simple frequency distributions and cross tabulations. Potential risk factors were then tested as predictors of symptom occurrence in a multiple logistic regression analysis (11). Risk factors were evaluated in a stepwise fashion with the best predictive model composed of variables significant at $p < 0.05$. All independent variables were categorical and stratified as follows: sex (M, F); age (5–9, 10–14); cooking stove fuel (gas, electric, or other); SES (I and II, III, IV, and V); maternal smoking (current, ex, and never); history of respiratory disease in either parent (yes, no); history of allergic disease in either parent (yes, no); person completing the questionnaire (mother, father, or other).

Results

Symptom and Illness Prevalence

Questionnaires were completed for 4,071 children (table 1). The combined rate of failure to return questionnaires and of parent refusal was 7.0% with no significant difference over the crude strata of air pollution areas (low, 7.0%; medium, 7.5%; high, 6.3%; $\chi^2_2 = 1.71$; $p = 0.19$). Fifty-three percent of the children were male, and the mean age was 9.4 yr (range, 5 to 14 yr) (table 1). Ninety-eight percent of the children were white (n = 3,985), closely reflecting Census Bureau data for the region. Nonwhite children were included in the analysis. Thirty-three percent of the families were in the high SES (I and II), 41% in the middle SES (III), and 25% in the low SES (IV and V).

Persistent wheeze and chronic cough were the most commonly reported

symptoms (table 2), but the prevalence of all respiratory symptoms was less than 10%. Most symptoms and illnesses were less frequent in the older age group (table 2). Chronic cough and chronic phlegm were reported significantly less often for older compared with younger females, but a similar pattern was not present in males. In contrast, the prevalence of persistent wheeze declined significantly with age for both sexes. The prevalence rates for both sexes of bronchitis, a history of chest illness before 2 yr of age, and chest illness in the past year were lower in the older age group, but no consistent association was present for age and ever-diagnosed asthma, hay fever, or pneumonia.

All symptoms and illnesses were significantly more frequent in children with a current or previous physician diagnosis of asthma (table 3). The prevalence of asthma was greater in males (4.5%) than in females (2.6%). However, when asthmatic and nonasthmatic children were considered separately, the prevalence of all respiratory symptoms evaluated was not affected by the

TABLE 1

AGE DISTRIBUTION OF CHILDREN'S SAMPLE POPULATION*

Age (yr)	Males (n)	Males (%)	Females (n)	Females (%)	Total
5–6	34	1.6	46	2.4	80
7	339	15.8	313	16.2	652
8	387	18.1	337	17.5	724
9	347	16.2	302	15.7	649
10	365	17.0	318	16.5	683
11	338	15.8	335	17.4	673
12	267	12.5	243	12.6	510
13–14	64	3.0	35	1.8	99
Total	2,141	(52.6)	1,929	(47.4)	4,070

* Age missing for 1 subject. Age distribution not significantly different by sex ($\chi^2_7 = 11.3$, $p > 0.05$).

TABLE 2

PREVALENCE (PER 100) OF RESPIRATORY SYMPTOMS AND ILLNESSES BY CHILD'S AGE AND SEX GROUP

	Male 5–9 yr	Male 10–14 yr	Female 5–9 yr	Female 10–14 yr	Total (n)
Respiratory symptoms					
Chronic cough	7.8	8.6	7.8*	6.3	8.8 (285)
Chronic phlegm	4.7	8.3	4.5*	2.1	4.2 (166)
Persistent wheeze	8.5*	7.5	7.2*	6.0	7.5 (300)
Illnesses					
Asthma, M.D. ever Dx	4.6	4.4	2.4	2.9	3.6 (143)
Hayfever, M.D. ever Dx	3.1	6.2	3.5	2.5	3.9 (154)
Pneumonia, M.D. ever Dx	13.4	12.2	11.3	10.6	11.9 (476)
Bronchitis, M.D. ever Dx	23.6*	19.9	21.1*	16.5	20.4 (818)
Severe chest illness < 2 yr age	10.8*	7.9	7.0*	5.3	7.9 (314)
Chest illness > 3 days in past year	12.6*	8.8	11.3	10.7	11.0 (445)

* $p < 0.05$ by chi square for difference between age groups within each sex.

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TABLE 3

PREVALENCE (PER 100) OF RESPIRATORY SYMPTOMS AND ILLNESSES BY CHILD'S SEX AND PHYSICIAN DIAGNOSIS OF CURRENT OR PREVIOUS ASTHMA*

M.D. Dx asthma (N)	Male		Female	
	Yes	No	Yes	No
	(94)	(1,995)	(49)	(1,823)
Respiratory symptoms				
Chronic cough	32.6	8.6	25.5	8.1
Chronic phlegm	25.8	3.9	22.9	2.9
Persistent wheeze	67.0	6.9	57.1	4.7
Illnesses				
Hayfever, M.D. ever Dx	25.0	3.8†	22.2	2.5
Pneumonia, M.D. ever, Dx	36.6	11.9	37.0	10.4
Bronchitis, M.D. ever Dx	48.4	20.7	47.8	18.3
Severe chest illness < 2 yr age	37.6†	8.0†	25.5	8.8
Chest illness > 3 days in past year	40.9	8.5	45.8	10.3

* Prevalence rates significantly different by chi square (p < 0.05) between asthmatics and nonasthmatics for all respiratory symptoms and illnesses within each sex.

† Prevalence rate of these illnesses significantly different (p < 0.05) between males and females within the same asthma status category.

child's sex. Only the prevalence of hay fever and of severe chest illness before 2 yr of age in children without asthma was significantly greater in male children.

Significant inverse trends with SES were present for chronic cough and severe chest illness before 2 yr of age (table 4). In contrast, physician-diagnosed hay fever and bronchitis, not specified as acute or chronic in the questionnaire, showed significant trends of increased prevalence with higher SES. No relationship was found between the remaining respiratory symptoms or illnesses and SES.

The multiple logistic analysis confirmed the independent association of younger age, male sex, and lower SES with an increased risk of chronic cough or phlegm and of persistent wheeze in the children (table 5). Male sex was also a risk factor for physician-diagnosed current or previous asthma in the logistic analysis.

Effects of the Person Completing the Questionnaire

Questionnaires were completed by the child's mother for 3,653 children (90.5%), by the child's father for 325 children (8.0%), and by an "other" person for 57 children (1.4%). Because patterns of responses from fathers and "other" persons were similar, the questionnaire data from these 2 sources were grouped in the following analyses of respondent bias. For simplicity we have referred to this respondent category as father-completed questionnaires. The sex and age distributions of children whose questionnaires were completed by mothers or fathers were comparable. Household characteristics of the 2 respondent categories, including parents' age, education, and smoking habits, were not significantly different. The prevalence rates for all respiratory illnesses and symptoms, except hay fever in the children, were higher when the questionnaire was completed by the mother than when completed by the father (table 6).

We also found that the responding parent's illness history was associated with the reported symptoms and illnesses for the child only in the mother-completed questionnaires (table 7). Bronchitis and emphysema were tested as a single variable for each parent because of their high correlation in the data. Mothers who gave a positive history of bronchitis or emphysema for themselves reported all symptoms and illnesses at higher rates for their children (p < 0.001) than did mothers who did not have a history of bronchitis or emphysema. In contrast, on father-completed questionnaires only bronchitis and chest illness in the past year in the child were associated with respiratory disease in the fathers. The remaining variables were not correlated with the father's history of respiratory disease. This association of respiratory illness in the parent completing the questionnaire and in the child may be confounded by parental smoking. However, the multiple logistic analysis confirmed the independent effect of respiratory disease in a parent on the variables studied (table 5). Similarly, the association of father-completed questionnaires with fewer symptoms reported for the child also persisted in the logistic analysis.

A reported history of allergy (asthma or hay fever) in the mother was similarly a significant (p < 0.001) independent risk factor for all respiratory symptoms and illnesses in the children, and a history of allergy in the father was a significant (p < 0.001) predictor for all outcomes tested except chest illness before 2 yr of age.

Environmental Exposures

To assess the effect of parental cigarette smoking, the children were grouped by the number of current parent smokers (table 8). Only households with cigarette smoking information for both parents were used. Significant linear associations were present between the number of parent smokers and the prevalence of chest illness in the past year, and of serious chest illness before 2 yr of age. A weaker and not significant association was present between parental cigarette smoking and chronic cough, and no association was present for either chronic phlegm or persistent wheeze. These stratified analyses were confirmed by the logistic models. Ma-

TABLE 4

PREVALENCE (PER 100) OF RESPIRATORY SYMPTOMS AND ILLNESSES BY SOCIOECONOMIC STATUS (SES)

	SES		
	I,II (High)	III (Medium)	IV,V (Low)
Respiratory symptoms			
Chronic cough*	6.5	7.3	8.0
Chronic phlegm	3.2	4.9	4.3
Persistent wheeze	6.4	6.6	6.3
Illnesses			
Asthma, M.D. ever Dx	3.4	3.9	3.5
Hayfever, M.D. ever Dx	6.2	3.3	1.8
Pneumonia, M.D. ever Dx	10.5	13.0	12.0
Bronchitis, M.D. ever Dx	22.8	21.8	19.9
Severe chest illness < 2 yr of age*	6.9	8.4	8.8
Chest illness > 3 days in past year	11.6	12.0	8.7

* χ² for linear trend significant (p < 0.05) and χ² for deviation from trend not significant (p > 0.05).

TABLE 5

VARIABLES ASSOCIATED WITH INCREASED RISK* OF RESPIRATORY SYMPTOMS OR DISEASE IN MULTIPLE LOGISTIC REGRESSION ANALYSIS

	Cough or Phlegm	Persistent Wheeze	Chest Illness in Last Year	Chest Illness Before 2 Yr of Age	M.D. Dx Asthma
Younger age	+	+	+	+	NS
Male sex	+	+	NS	NS	+
Lower SES	+	+	NS	NS	NS
Parent Hx allergy†	+	+	+	+	+
Parent Hx respiratory disease‡	+	+	+	+	+
Mother-completed questionnaire	+	+	NS	+	NS
Maternal smoking	NS	NS	+	+	NS
Gas cooking stove	NS	NS	NS	NS	NS

Definition of abbreviations: SES = socioeconomic status; NS = not significant.
* p < 0.05.
† Parent Hx allergy defined as asthma or hay fever in either parent.
‡ Parent Hx respiratory disease defined as emphysema or bronchitis (not specified as acute or chronic) in either parent.

ternal smoking was a significant independent risk factor for chest illness in the past year and serious chest illness before 2 yr of age but not for physician-diagnosed current or previous asthma (table 5).

Smoking questionnaires were completed by 1,906 children in Grades 4 through 6. Four hundred ninety-eight children (26.1%) admitted to trying at least a few puffs, but only 53 (2.7%, 39 boys and 14 girls) said they had ever smoked 5 or more cigarettes, and currently smoked. Parents reported chronic cough in 2 of 52 "current children smokers" and persistent wheeze in 4 of 51 "smokers." The number of symptomatic current smoking children was small, and the rates were not significantly different from the age- and sex-adjusted rates for the entire sample.

Gas cooking stove use was significantly associated (inversely) with SES. Gas was used as fuel for cooking in the homes of 62.1% of the low SES, 53.8% of middle SES, and 45.2% of the high SES children. When gas cooking stove use was tested in the multiple logistic model, a significant association was not present between gas stove use and any of the respiratory or illness variables after adjusting for SES.

Discussion

We have evaluated respiratory illness and symptom prevalences in 4,071 children 5 to 14 yr of age using a new parent-completed standardized questionnaire (ATS-DLD-78-C). The study population was selected from a representative sample of area schools, and a very high response rate was achieved. The questionnaire performed satisfactorily and most items were appropriately completed. The missing response rate was highest for questions concerning parental history, which are located at the end of the questionnaire. Personal cigarette smoking histories were obtained directly from children in the fourth through sixth grades, but the responses were not validated.

The prevalence rates of respiratory symptoms in this population were low and similar to the rates in nonsmoking adults in the same area (12). The prevalences of most symptoms and illnesses are also similar to other large studies of children, but strict comparisons are difficult because of differences in questionnaire wording and population characteristics (1, 2, 13-16).

Several risk factors were demonstrated to be independently associated with the respiratory outcomes. In agreement with findings from cross-sectional surveys in the United States (1, 2), England (4, 13, 14), and Australia (6, 15), most of the symptoms and illnesses were significantly more prevalent in male children. Prospective surveillance studies of lower respiratory tract infections have also demonstrated a greater incidence rate in male children (17-19).

All symptoms and chest illnesses were more prevalent in the younger children (table 2). The finding of lower prevalence with increased age confirms the findings from other cross-sectional (2, 3, 6) and prospective studies (17, 19). This pattern of symptom variation with age and sex is paralleled by mortality rates for respiratory disease in children (14, 20, 21).

TABLE 6

PREVALENCE (PER 100) OF REPORTED RESPIRATORY SYMPTOMS AND ILLNESSES BY PERSON COMPLETING QUESTIONNAIRE

	Mother Completed (n = 3,853)	Father Completed (n = 382)
Respiratory symptoms		
Chronic cough*	9.4	3.3
Chronic phlegm	4.1	2.0
Persistent wheeze*	7.1	4.0
Illnesses		
Asthma, M.D. Dx	3.6	3.0
Hayfever, M.D. Dx	3.9	4.0
Pneumonia, M.D. Dx*	12.4	8.2
Bronchitis, M.D. Dx*	22.2	16.8
Severe chest illness before 2 yr of age*	8.4	4.4
Chest illness > 3 days in past year	11.3	8.2

* p < 0.05.

TABLE 7

PREVALENCE (PER 100) OF RESPIRATORY SYMPTOMS AND ILLNESSES IN CHILDREN BY RESPIRATORY DISEASE STATUS OF PERSONS COMPLETING THE QUESTIONNAIRE

	Mother-Completed Questionnaire		Father-Completed Questionnaire	
	Respiratory Disease In Mother		Respiratory Disease In Father	
Symptom or Illness In Child	Yes	No	Yes	No
Respiratory symptom				
Chronic cough	10.5*	8.2	3.4	3.2
Chronic phlegm	7.0*	3.8	1.8	2.1
Persistent wheeze	12.1*	6.2	3.3	4.1
Illnesses				
Asthma, M.D. Dx	5.7*	3.0	0.0	2.4
Hayfever, M.D. Dx	6.2*	3.2	3.2	4.2
Pneumonia, M.D. Dx	17.7*	10.7	10.9	7.3
Bronchitis, M.D. Dx	37.2	20.7	34.4*	12.6
Severe chest illness before 2 yr of age	14.3*	6.8	3.2	3.1
Chest illness > 3 days in past year	20.0*	8.6	17.2†	6.2

* p < 0.001.
† p < 0.05 for differences in reported prevalence of child's illnesses between presence and absence of respiratory disease in parent completing questionnaire, e.g., in mother-completed questionnaires, mothers who reported respiratory disease in themselves reported significantly more symptoms and illnesses in their children than did mothers who did not report respiratory disease in themselves.

TABLE 8

PREVALENCE (PER 100) OF REPORTED
RESPIRATORY SYMPTOMS AND ILLNESSES
BY CURRENT PARENT CIGARETTE SMOKERS

	Number of Current Parent Smokers		
	0	1	2
Respiratory symptom			
Chronic cough	8.3	7.0	8.3
Chronic phlegm	4.1	4.3	4.0
Persistent wheeze	7.2	7.7	8.4
Illnesses			
Severe chest illness before 2 yr of age*	8.7	7.9	11.5
Chest illness > 3 days in past year*	8.3	11.3	13.6

* χ^2 for linear trend significant ($p < 0.05$) and χ^2 for deviation from trend not significant ($p > 0.05$).

In this study, chronic cough and chest illness before 2 yr of age were inversely associated with SES, but a positive association was found between SES and physician-diagnosed bronchitis. British studies have shown an inverse gradient of respiratory illness rates with social class (3, 5, 14). A significant inverse association of social class and respiratory illness in the last year and before 2 yr of age has also been found in a large prevalence survey in the United States (22).

It is not clear how SES modifies respiratory symptoms or illnesses. Several factors, such as family size or crowding, not considered specifically in this study, have been shown to correlate with childhood illness rates and may partially explain the effect of SES (17). The small positive association of SES and physician-diagnosed bronchitis may be due to better access to medical care and not to differences in disease rates. This trend is opposite to the inverse association of SES and chronic phlegm production in our population and suggests that physician-diagnosed bronchitis may not be an appropriate measure of actual rates of bronchitis.

Other studies have noted a positive association of atopy and social class similar to our association of hay fever and SES. However, a consistent association has not been noted between asthma and social class (15, 23, 24).

Respondent Bias

The validity of results from questionnaire studies may be altered by biases introduced by the observer or by the respondents (2, 4, 25, 26). The recent use of standardized questionnaires has largely eliminated significant observer bias (27), but bias introduced by re-

spondents remains a potential source of systematic error. We found most respiratory illnesses and symptoms to be reported significantly less frequently by the fathers than by the mothers (table 4). No consistent differences that might explain this observation were present in the reporting parent's age, education, smoking status, or household SES. The difference in reporting illness rates persisted in the logistic analysis. While we do not have validation of the reported illnesses by other criteria, the finding appears to result from underreporting by the fathers. The prevalence rates of illnesses in children whose mothers completed the questionnaires were closer to rates in other studies (1, 2).

This bias in reporting may be due to less observation of the child by the working father, less treatment by the father of children's health-related complaints, or a different perception by fathers of respiratory symptoms in their children. Parental reporting differences were greatest for symptoms but were not present for some illnesses (table 6). This discrepancy suggests that fathers may have knowledge of their children's more severe illnesses but not of less disabling symptoms. In two-parent families, questionnaires should be completed by the mother, and the presence of bias should be evaluated in questionnaires completed by the father or other persons.

Higher symptom prevalences in children were significantly associated with a reported history of respiratory disease in either parent (tables 5 and 7). The association, which was independent of maternal smoking status in the logistic analysis, was consistently found with mother-completed questionnaires but not with symptoms and most illnesses in father-completed questionnaires. The correlation of reported respiratory disease status in parents and children, not explained by passive smoking and other known risk factors, may be due to genetic factors, a common exposure to air pollution or other environmental agents, or to overreporting (bias) by symptomatic parents for their children. By reporting bias, we mean that parents who report respiratory symptoms in themselves are more likely to report them in their children.

Respiratory symptoms in the parents partially explained an apparent association of passive smoking and childhood symptoms in a study by Lebowitz and Burrows (28). Other studies have failed to consider this possible source

of bias (29, 30). Reporting bias is an important consideration in parent-completed questionnaires and should be evaluated, if possible, when questionnaires are used for data collection.

A history of severe chest illness before 2 yr of age was reported significantly more often for younger children. This association probably represents a recall bias by the reporting parents, i.e., parents with younger children are closer in time to the early illnesses of their children and recall them at a greater rate than parents of older children. Recall biases are also a problem in cross-sectional studies because parents of symptomatic children may preferentially recall childhood illnesses (20).

Environmental Risk Factors

Environmental variables were tested for significant contributions to the logistic model that controlled for other known risk factors (age, sex, SES, reporting parent, parent history of respiratory disease). Passive smoking was independently associated with chest illness in the past year and before 2 yr of age after adjustment for known risk factors and for reporting biases (table 5). In addition, the association was present when considering only parents who did not report respiratory disease. Passive smoking was not a risk factor for chronic cough, phlegm, or wheeze. We did not confirm the finding of Gortmaker and coworkers (31) of an increased risk of asthma in children of smoking parents.

The association of passive smoking and chronic chest illness before 2 yr of age in our data is consistent with the results of studies reporting an increased incidence of respiratory illnesses in young children of cigarette smoking mothers (32-35). Ferguson and associates (32) found an increased risk of lower respiratory illness and maternal smoking that declined over the first 2 yr of life and had disappeared by the third year. Several investigations have demonstrated an increased prevalence of respiratory symptoms or illnesses in exposed school-age children, but these studies have often failed to adjust for social class, respondent bias, or for smoking by the children themselves (29, 36, 37), factors which may alter the observed associations.

Weiss and coworkers (2) found that wheeze in children 5 to 9 yr of age was correlated with maternal smoking and was independent of parental respira-

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tory symptoms. We did not confirm this finding in our larger sample. This difference may be due to different home exposures to passive smoke in the 2 populations (urban versus rural), or to other differences such as amount of smoking in the presence of children. Urban populations on average smoke more than rural populations, and this may result in higher exposure levels (37). The effect of passive smoking on children's respiratory symptoms or pulmonary function has not been directly correlated with indoor concentrations of specific pollutants from passive smoking.

We did not find gas cooking stoves to be an independent risk factor for any chronic respiratory symptoms or illnesses. Speizer and associates (22) reported an association of gas cooking stoves with serious respiratory illness before 2 yr of age, but analysis of the cohort with additional subjects has not confirmed the initial finding (1). Melia and Florey and coworkers (38) and Florey and coworkers (39) found an independent association of respiratory symptoms or disease prevalence in children and the use of gas cooking stoves. Prevalence was not related to kitchen NO_2 levels but was correlated with concentrations of NO_2 in the children's bedrooms. The NO_2 concentrations in homes with gas stoves are significantly higher than outdoors or in homes with electric stoves (40), but the health effects, if any, of this observation remain to be resolved.

In summary, parent-completed questionnaires for 4,071 children living in a rural area have demonstrated several independent risk factors for respiratory symptoms and illnesses. Younger age, male sex, and lower SES were risk factors for all symptoms tested and for some of the illness outcomes. A history of allergy or respiratory illness in either parent was an independent risk factor for all outcomes, indicating a reporting bias and possibly common genetic factors or environmental exposures. Parental cigarette smoking was associated with chest illnesses but not with chronic respiratory symptoms in the children. Response biases caused by preferential recall of early illness in younger children and to completion of the questionnaire by fathers also was demonstrated. No significant association of gas stoves and respiratory symptoms was found.

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"Relationship of Parental Smoking and Gas Cooking to Respiratory
Disease in Children" Chest 64: 662-668, 1983.

SUMMARY: In a survey of 1,355 children six to 12 years of age, the
risk of hospitalization for respiratory illness among children
before age two years was increased when gas was used for cooking
at home (p < 0.001) or at least one of the parents smoked
(p < 0.02). The occurrence of cough with colds in children was
also significantly increased when one or both parents smoked
(p < 0.001). Small but significant increases (p < .05) in the mean
values of forced expiratory volume at one second, the flow rate of
75 percent of the forced vital capacity, and the forced expiratory
flow rate from 25 percent to 75 percent of the vital capacity (FEF
25-75) were seen after administering inhaled isoproterenol to
children whose parents smoked (n = 94) but not among children whose
parents did not smoke (n = 89); this was not seen in association
with gas cooking. Thus, exposure of children during the first two
years of life to gas cooking or cigarette smoking appears to be
associated with an increased risk of hospitalization for respiratory
illness, and cigarette smoking appears to be associated with a more
consistent response to inhaled bronchodilator among six - to 12-
year-old children with no other history of chronic respiratory
illness.

Relationship of Parental Smoking and Gas Cooking to Respiratory Disease in Children*

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In a survey of 1,355 children six to 12 years of age, the risk of hospitalization for respiratory illness among children before age two years was increased when gas was used for cooking at home (p < 0.001) or at least one of the parents smoked (p < 0.02). The occurrence of cough with colds in children also was significantly increased when one or both parents smoked (p < 0.001). Small but significant increases (p < .05) in the mean values of forced expiratory volume at one second, the flow rate at 75 percent of the forced vital capacity, and the forced expiratory flow rate from 25 percent to 75 percent of the vital capacity (FEF25-75) were seen after administering inhaled isoproterenol to children whose parents smoked (n = 94) but not among children whose parents did not smoke (n = 89); this was not seen in association with gas cooking. Thus, exposure of children during the first two years of life to gas cooking or cigarette smoking appears to be associated with an increased risk of hospitalization for respiratory illness, and cigarette smoking appears to be associated with a more consistent response to inhaled bronchodilator among six- to 12-year-old children with no other history of chronic respiratory illness.

Parental smoking has been shown to be related to increased risk of respiratory illness in children during the first year of life,[1,2] and to an increased risk of morning cough, respiratory infections, and breathlessness among older children.[3,4] Specifically, an increased incidence of pneumonia and bronchitis with consequent hospitalizations has been reported among infants whose parents smoked compared to children whose parents did not smoke.[5] Parental smoking also has been reported to increase the risk of persistent wheeze[6] and symptomatic asthma.[7] In a study of British secondary schoolchildren that showed early morning cough to be more commonly reported by children who smoked, the effect on these smoking children of parental smoking appeared to be additive.[8] A decrease in pulmonary function measurements also has been noted in nonsmoking children whose parents smoked.[9,10]

An association has been similarly shown between respiratory illness in children and gas cooking, apparently from increased levels of nitrogen dioxide and nitric oxide in the homes with gas stoves.[11,12] In addition, pulmonary function measurements performed in school age children were found to be lower in association with the use of gas stoves in the home.[13,14]

The current study was designed to further examine the relationship of parental smoking and gas cooking on the occurrence of respiratory illness and symptoms in children from a midwestern university community. Additionally, we examined the relationship between these environmental exposures and pulmonary functions.

METHODS

Subjects

Children, ages 6 to 12, who attended primary school in the Iowa City School District were contacted after permission was obtained from school administrators. The school district serves a university community. The children were therefore generally from middle and upper social classes. Participating schools included approximately 87 percent of the 2,062 children six to 12 years of age enrolled in the school district. Children from the participating schools were sent home with a letter explaining to parents the purpose of the studies, the information we were interested in collecting and why. The parents were requested to complete a modification of the questionnaire developed by the American Thoracic Society (ATS) for the Division of Lung Disease (DLD) of the National Heart, Lung, and Blood Institute (the ATS-DLD questionnaire)[15] and to return it to us in a stamped, self-addressed envelope. (A copy of the modified questionnaire is available on request from the authors.) Two weeks following the initial distribution of the questionnaires to the parents, another letter was sent as a reminder to parents who had failed to return a completed questionnaire.

In order to determine if nonrespondent parents and their children differed significantly in certain characteristics from those parents who had completed the questionnaires about their children, 200 nonrespondent parents were randomly selected and contacted by telephone by a trained research assistant four weeks after the questionnaires were initially sent to the parents. The parents were each read the part of the questionnaire that related most directly to cigarette smoking and respiratory illness. To ensure that the questions were answered accurately, these pertinent questions from the questionnaire were read aloud exactly as printed and without any elaboration by the research assistant.

Pulmonary Function Measurements

Pulmonary function measurements were obtained from 89 chil-

dren (47 girls and 41 boys) whose parents did not smoke and 94 children (52 girls and 42 boys) whose parents smoked. These children were randomly selected using tables of random numbers from the children for whom complete information was obtained using the questionnaire. All parents were requested to indicate their consent for pulmonary function studies to be obtained from their children, after we had provided a full written explanation of the reasons for obtaining the measurements and the procedures the child would follow during pulmonary function testing. Consent was obtained from 411 (85.6 percent) of the 484 children whose parents did not smoke and 596 (91.1 percent) of the 654 children whose parents smoked. When parental smoking was kept constant, the proportions of children who had cough with cold, cough apart from colds, or phlegm with or apart from colds were not significantly different for consenting parents compared to nonconsenting parents. We therefore felt that our sampling procedure produced a representative population of children.

Children were excluded if there was a history of recurrent respiratory illness or if there was any history of upper or lower respiratory infection during the prior six months. Spirometry was measured with a Jones Pulmonor waterless respirometer. Calculations of the parameters measured were done by the Jones Datamatic Computer with daily calibration. Lung volumes were measured by use of a plethysmograph (model 2000B Cardiopulmonary Instruments) using a 3 L/second Fleisch temperature-controlled pneumotach, with a flow accuracy of ± 1 percent of full scale.

Each child was instructed in the measurement maneuver and was in an upright sitting position. Each test was repeated three to five times, and the best effort was taken. Flow rates and lung volumes were measured before and five minutes subsequent to 1.25 mg inhaled isoproterenol diluted with 2 ml normal saline solution and administered by an open nebulizer.

Analysis of Data

Discrete multivariate analysis was used to study the interactions among factors. In this analysis, maternal and paternal smoking and gas cooking were treated as independent factors, while the frequencies of various respiratory symptoms or illness were the dependent variables. The reported prevalence of respiratory symptoms or illnesses were stratified by parental smoking (mother alone, father alone, both parents, either or both parent smokes, neither parent smokes) and by cooking fuel use. Odds ratio was calculated for each interaction effect. Odds ratios greater than one indicated that the variable had a higher risk for the children and conversely odds ratios of less than one indicated lower risk. A chi-square analysis was used to examine the significance of the odds ratio.

Regression lines were fitted to each of the pulmonary function measurements using the Statistical Analysis System (SAS) using the stepwise procedure. The variables entered in the equation were

age in years, sex, weight (kg), and standing height (cm). Lines were fitted separately for children from smoking and nonsmoking environments, as well as for values obtained by pooling these two groups. F-tests were performed as described by Neter and Wasserman to compare the fit of the lines obtained for values for children from the two environments and for the pooled data. Paired t-tests were used to compare the prebronchodilator and postbronchodilator pulmonary functions.

RESULTS

Completed questionnaires were obtained for 1,355 children, or 65.7 percent of the children six to 12 years of age in the school district. Of the 1,355 completed questionnaires, data on parental smoking history was complete for 1,138 (84 percent) of the children. In the remaining 217 questionnaires, either maternal or paternal or both smoking histories were unrecorded or incompletely recorded. The proportion of children with incomplete or no parental smoking history who had cough with or apart from colds, congestion or bringing up phlegm, or had chronic lung diseases was not statistically significantly different from the proportion of children with parental smoking histories who had these symptoms. These questionnaires were eliminated in subsequent analysis. Forty-nine percent of these children were males, and 51 percent were females. Five percent of the children had established diagnoses of chronic respiratory diseases. Two had cystic fibrosis, one had pulmonary tuberculosis, two had diagnoses of chronic bronchitis, and 49 had asthma. When we compared the 200 randomly selected nonrespondent families to our study population, we found no statistically significant differences in the proportion of parents who smoked at home. The proportions of children who had cough with colds, cough apart from colds, or who had congestion or bringing up phlegm with or apart from colds were not significantly different among the two groups.

Fifteen percent of the parents completing the questionnaire indicated they had bronchitis, emphysema, asthma, or other chronic respiratory condition. We found no relationship between the report of chronic respiratory illness in parents and the reported prevalence in children of symptoms of cough with colds,

Table 1—*Proportion of Children with Cough with Colds or Hospitalized for Chest Problems Before Age 2 Years, by History of Parental Smoking and Home Cooking Fuel Used*

Home Cooking Fuel	Parental Smoking History (Yes = Parent Smokes)		Percentage of Children Affected (Total Number of Children in the Group)	
	Father	Mother	Cough With Colds	Hospitalization For Chest Illnesses
Gas	No	No	32.8 (137)	5.1 (138)
Gas	No	Yes	35.7 (28)	7.1 (28)
Gas	Yes	No	35.6 (101)	8.0 (100)
Gas	Yes	Yes	30.6 (111)	9.8 (112)
Electricity	No	No	28.9 (343)	2.1 (341)
Electricity	No	Yes	37.7 (69)	8.8 (68)
Electricity	Yes	No	37.7 (69)	5.6 (178)
Electricity	Yes	Yes	44.5 (73)	1.2 (172)

Table 2—*Association of Parental Smoking and Gas Cooking with Hospitalization of Children Before Age 2 Years for Respiratory Illnesses*

Independent Variables	No. of Children Hospitalized for Chest Illnesses		Odds Ratio	SE	p-Value
	Yes	No			
Fuel used for home cooking					
Gas	28	350	2.4	0.684	0.001
Electricity	25	736	1.0	...	...
Parental smoking					
Father alone smokes	18	260	2.3	0.856	0.022
Mother alone smokes	8	90	2.9	1.239	0.026
Father and mother smoke	13	271	1.6	0.856	0.21
Either or both parents smoke	39	621	2.1	0.666	0.017
Neither parent smokes	14	465	1.0	...	...

cough apart from cold, or bringing of phlegm with cough apart from colds. Of the 1,135 children, 31 percent lived in homes where gas was used for cooking, and 69 percent lived in homes where electricity was used for cooking. There was a significant association between parental smoking and the use of gas for cooking. Fathers smoked in 224 (56.4 percent) of the 397 homes where gas was used for cooking, compared to 366 (46.6 percent) of the 786 homes in which electricity was used for cooking ($x^2 = 10.28$, $p < 0.001$). Similarly, mothers smoked in 180 (40.8 percent) of the 441 homes in which gas was used for cooking, compared to 292 (33.7 percent) of the 866 homes in which electricity was used for cooking ($x^2 = 6.33$, $p < 0.05$). The proportion of children with chronic respiratory symptoms by parental smoking and use of cooking fuel are shown in Table 1.

The use of gas for cooking was associated with an increased risk of hospitalization of the children before age two years because of chest colds and other respiratory illnesses (odds ratio = 2.4) independent of parental smoking (Table 2). Any parental smoking also increased the odds ratio. When both parents smoked in a household in which gas was used for cooking, the odds ratio was 9.25 ($p = 0.0006$). The use of gas for cooking was not associated with increased risk of occurrence of cough with colds in the children. How-

ever, parental smoking increased the risk of occurrence of these symptoms (Table 3). Other than the possibility of wheezing and whistling sounds in the chest with colds, none of the dependent variables in Table 4 was significantly associated with parental smoking and/or use of gas for cooking. Also, the frequency of occurrence of ear infections in the children between ages 0 to two years, or two to five years, or the occurrence of wheezing with exercise was not found to be associated with parental smoking or use of gas for cooking.

The mean standing height of 144.2 cm and weight of 37.8 kg for children whose parents smoked was not significantly different from the mean standing height of 145.6 cm and weight of 38.7 kg for children whose parents did not smoke. Mean values for initial measurements of pulmonary function before the inhaled isoproterenol did not differ significantly between children from smoking and non-smoking families. Significant differences in mean values were not seen after bronchodilator inhalation in the children from non-smoking families or were not seen among children from smoking families for the measurements of FEF75, FEV, and FEF25-75 (Table 5). The mean values of the measurements of lung volumes for the two groups of children were not statistically different. Because 28 t-tests were performed for these analyses, adjustment was made by accepting only t-tests with p

Table 3—*Association of Parental Smoking and Gas Cooking with Occurrence of Cough with Colds in Children*

Independent Variables	No. of Children with Symptoms of Coughs with Colds		Odds Ratio	SE	p-Value
	Yes	No			
Fuel used for home cooking					
Gas	125	252	0.9	0.123	0.55
Electricity	266	495	1.0	...	...
Parental smoking					
Father alone smokes	100	177	1.4	0.228	0.023
Mother alone smokes	36	61	1.5	0.348	0.084
Father and mother smoke	111	173	1.6	0.255	0.002
Either or both parents smoke	247	411	1.5	0.194	0.001
Neither parent smokes	144	366	1.0	...	...

Table 4—Relationship of Parental Smoking and Cooking Gas with Occurrence of Respiratory Symptoms in Children

Independent Variable	No. of Children with Respiratory Symptoms		Odds Ratio	± SE	p-Value
	Yes	No			
1. Chest congestion and phlegm with colds					
Gas	70	307	1.1	0.188	0.41
Electricity	126	633	1.0	...	...
Father alone smokes	46	230	1.0	0.213	0.82
Mother alone smokes	19	78	1.3	0.363	0.40
Father and mother smoke	54	229	1.2	0.383	0.28
Either or both parents smoke	119	537	1.2	0.186	0.35
Neither parent smokes	77	403	1.0	...	...
2. Chest congestion and phlegm apart from cold					
Gas	17	345	1.0	0.302	0.99
Electricity	35	708	1.0	...	...
Father alone smokes	12	258	0.9	0.345	0.86
Mother alone smokes	7	87	1.6	0.730	0.30
Father and mother smoke	11	264	0.8	0.317	0.64
Either or both parents smoke	30	609	1.0	0.286	0.98
Neither parent smokes	22	444	1.0	...	...
3. Wheezing and whistling sounds in chests with colds					
Gas	104	273	1.0	0.154	0.56
Electricity	198	564	1.0	...	...
Father alone smokes	74	202	1.2	0.210	0.27
Mother alone smokes	30	67	1.5	0.362	0.12
Father and mother smoke	86	198	1.4	0.241	0.03
Either or both parents smoke	190	467	1.3	0.165	0.03
Neither parent smokes	112	370	1.0	...	...
4. Wheezing and whistling sound in chest apart from colds					
Gas	29	326	0.9	0.222	0.80
Electricity	61	647	0.1	...	...
Father alone smokes	24	235	1.2	0.329	0.52
Mother alone smokes	14	73	2.2	0.761	0.02
Father and mother smoke	16	244	0.6	0.239	0.39
Either or both parents smoke	54	552	1.1	0.257	0.55
Neither parent smokes	36	421	1.0	...	...
5. Attacks of wheezing with shortness of breath					
Gas	30	346	0.7	0.158	0.12
Electricity	83	679	1.0	...	...
Father alone smokes	26	251	0.8	0.211	0.48
Mother alone smokes	12	85	1.1	0.389	0.70
Father and mother smoke	22	261	0.7	0.181	0.14
Either or both parents smoke	60	597	0.8	0.161	0.29
Neither parent smokes	53	428	1.0	...	...

values of <0.002 as significantly different at a 0.05 confidence level (0.05 ÷ 28 = 0.002). The mean percentage changes in the pulmonary function measurements (calculated as the differences between the postvalue and prevalue divided by the prevalues for each patient), however, did not differ significantly between the two groups of children (using an unpaired t-test).

Discussion

Respiratory symptoms and illnesses occur frequently, particularly in the temperate regions of the worlds in preschool and school-age children. Only recently has it been appreciated that parental smoking at home may be associated with an increased risk of occurrence of respiratory symptoms in children. A higher rate of hospitalization of the children before age two years for chest illnesses (bronchitis, pneumonia, etc) was associated with both parental smoking and gas cooking. A significant increase in pulmonary function after an inhaled bronchodilator among children of

Table 5—*Flow Rates of Children Before and After Inhaled Isoproterenol*

| Variables | Children of Smoking Parents | | | Children of Nonsmoking Parents | | |
| | Mean (SE) Measurements of Flow Rates and Lung Volumes | | | Mean (SE) Measurements of Flow Rates and Lung Volumes | | |
	Preisoproterenol	Postisoproterenol	p*	Preisoproterenol	Postisoproterenol	p*
PEFR	5.11 (0.13)	4.97 (0.13)	0.11	5.10 (0.13)	5.05 (0.12)	0.42
FEF25	4.18 (0.12)	4.15 (0.12)	0.71	4.34 (0.11)	4.23 (0.1)	0.11
FEF50	3.22 (0.09)	3.35 (0.09)	0.02	3.25 (0.09)	3.36 (0.09)	0.07
FEF75	1.52 (0.05)	1.76 (0.07)	0.0001†	1.56 (0.06)	1.69 (0.07)	0.11
FEV₁	2.23 (0.05)	2.27 (0.05)	0.0002†	2.21 (0.05)	2.23 (0.06)	0.34
FEV	2.52 (0.06)	2.52 (0.06)	0.48	2.47 (0.06)	2.50 (0.07)	0.17
FEF25-75	2.60 (0.08)	2.82 (0.08)	0.0001†	2.60 (0.07)	2.78 (0.09)	0.03
FVC	2.55 (0.06)	2.57 (0.06)	0.18	2.51 (0.07)	2.53 (0.07)	0.13

*Paired t-test comparing initial pulmonary function measurements and postbronchodilator values.
†Significant at 0.05 level after adjusting for the performance of 28 t-tests.

smoking parents is an interesting additional observation perhaps consistent with previous reports of increased bronchial reactivity in cigarette smokers with normal lung function and an association between symptomatic asthma in children and parental smoking.

Parental smoking may be associated with different types of respiratory illnesses in infancy compared to the school age. Fergusson et al found an increased risk of infantile lower respiratory illnesses in the last eight months of the first year of the infant's life to be associated with maternal but not paternal smoking. Similarly, Colley et al found that infantile pneumonia was more common when both parents smoked than when neither parent smoked. The risk was intermediate when only one parent smoked. These results are consistent with our findings that hospitalization of children in the first two years of life for bronchitis and pneumonia was associated with parental smoking. However, Fergusson et al did not study the association of parental smoking and use of gas for cooking on respiratory infection rates. Their study is different from ours also, in that they studied respiratory infection rate between four and 12 months of life. Their study was prospective-retrospective in design, and therefore, parental recall may have been more reliable than in our study. In the first year of life, an infant is likely to spend proportionately more time with the mother than the father. Thus, the age of the child at the time of the administration of the respiratory questionnaire may have been an important factor in the finding that maternal but not paternal smoking was associated with respiratory illness in the child.

Weiss et al reported a dose response between prevalence rate of symptoms of persistent wheezing, cough, and phlegm in children and parental smoking. The rate of occurrence of symptoms in children was highest when both parents smoked, intermediate when either parent smoked, and lowest when no parent smoked. However, the authors also found a strong association between the occurrence rate of these symptoms in the children and the prevalence rate for such symptoms in the parents. We found a significant association between parental smoking and the prevalence of cough with colds in the children. However, we did not find any association between parental smoking or the use of gas cooking and the reported incidence of cough apart from colds and chest congestion and bringing up phlegm with or apart from colds. In a study of children whose ages were similar to the children in our population, however, Colley found an association between parental smoking and the occurrence of cough during the day or at night in winter in the children. He also found an association between parental smoking and bringing up "any phlegm from the chest first thing in the morning in winter" by the children. The lack of association between these variables and parental smoking in our study may be attributable to the phrasing of the questions in the ATS-DLD questionnaire, where "in the morning" was not specifically mentioned, and where phlegm production was sought in association with chest colds rather than "in winter." Slight changes in the phrasing of questions can result in substantial differences in the type of responses one obtains.

Flory et al showed an association between the levels of NO₂ in kitchens and bedrooms of the homes, and the prevalence of respiratory illness in primary schoolchildren. This association was independent of the children's age, sex, social class, and the number of cigarettes smoked at home. In another study, children six to 11 years old from households with gas stoves had a history of more frequent respiratory illnesses before age two years compared to children from homes where gas was not used for cooking. In a study of schoolchildren in England and Scotland, a reported incidence of coughs, colds going to the chest, and bronchitis in children from homes using gas for cooking

was significantly higher than for children from homes where electricity was used.[11] Melia et al[12] demonstrated that the association between respiratory illness and gas cooking tended to disappear as the children grew older.

The nature of the association of respiratory symptoms in children and gas cooking in the home is yet unclear. Two oxides of nitrogen, nitric oxide (NO) and nitrogen dioxide (NO_2), are produced in varying concentrations in homes with gas stoves.[13-15] It has been observed that acute exposure of man and animals to high levels of nitrogen dioxide (NO_2) can cause pulmonary edema and death.[16]

A significant reduction in FEF25-75 values was observed in children who smoked, as well as in children whose parents smoked but who were non-smokers themselves.[17] At least one group of investigators has found no association between parental smoking and lung function measurements of the children.[17] In these studies, the children did not receive an inhaled bronchodilator drug. Inhaled bronchodilator medication was administered to children in our study, and we observed statistically significant differences in the mean values of FEF75, FEV_1, and FEF25-75 for children whose parents smoked compared to those whose parents did not smoke. The clinical importance of such observed differences in the absolute values of pulmonary function measurements is, however, unclear.

In a recent study of children six to 11 years old from households with gas stoves, small but significant differences were found in FEV, and FVC corrected for height, compared to children from homes where gas was not used for cooking.[5] These families tended to be poorer and were in the lower socioeconomic class. Flory et al[5] found no significant relationship between lung function measurements and concentrations of NO_2 in either kitchen or bedroom. Lung function measurements of peak expiratory flow rates (PEFR) and FEF25-75 for children from homes with gas stoves were not significantly higher than measurements for children from homes with electric stoves. Hasselblad et al[12] however, found pulmonary function suggestively decreased among nine- to 13-year-old girls in homes with gas stoves and not among younger children.

Based on the findings of this report and from previously published findings, one is led to conclude that parental smoking is associated with a risk of certain respiratory illnesses and symptoms among children living in the same environment. An independent but similar effect is suggested for gas cooking. Children from homes where parents smoke had increased reactivity of airways after bronchodilator therapy, but it is not known if these changes persist or have clinical consequences.

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Myocardial Protection via the Coronary Sinus

The First International Symposium on Myocardial Protection via the Coronary Sinus will be held at the Hotel InterContinental Vienna, Vienna, Austria, February 27-29, 1984. For information, contact the Secretariat, c/o Interconvention, PO Box 80, A-1107 Vienna, Austria.

Diagnostic Imaging

The Department of Radiology, Duke University Medical Center, will present this five-day postgraduate course at the Hyatt Regency Cancun Hotel, Cancun, Mexico, February 12-17, 1984. For information, contact Donald R. Kirks, M.D., Department of Radiology, Duke University Medical Center, Box 3834, Durham, North Carolina 27710 (919:681-2711, ext 286 or 287).

Parental Smoking and Gas Cooking in Respiratory Disease of Children (Eland et al)

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ABSTRACT. A total of 131 infants were monitored from birth through
the first year of life for respiratory viral infection and illness
and evaluated for the relationship that these had to certain social
and familial factors. The results showed no general patterns of
association between viral infection and the study factors, but
there were several significant individual associations. Excess
influenza virus infection was found for black infants, infants
with at least one sibling, and especially those with school age
siblings. Rhinovirus infection rates were highest among girls
attending daycare. In addition, significantly higher rates of
lower respiratory disease (LRD) were seen in daycare infants and
low socioeconomic infants and a definite trend to increasing amounts
of LRD was seen with increasing family size. Protection from LRD
seen in girls was apparently lost in daycare. No convincing
differences for viral infection or respiratory illness were seen
with parental smoking as an isolated factor.

MARCH (1)

Effects of social and family factors on viral respiratory infection and illness in the first year of life

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SUMMARY   A total of 131 infants were monitored from birth through the first year of life for respiratory viral infection and illness and evaluated for the relationship that these had to certain social and familial factors. The results showed no general patterns of association between viral infection and the study factors, but there were several significant individual associations. Excess influenza virus infection was found for black infants, infants with at least one sibling, and especially those with school age siblings. Rhinovirus infection rates were highest among girls attending daycare. In addition, significantly higher rates of lower respiratory disease (LRD) were seen in daycare infants and low socioeconomic infants and a definite trend to increasing amounts of LRD was seen with increasing family size. Protection from LRD seen in girls was apparently lost in daycare. No convincing differences for viral infection or respiratory illness were seen with parental smoking as an isolated factor.

Viral respiratory illness is a major cause of morbidity and mortality in infancy. Children under 1 year of age have the highest incidence of acute respiratory illness[1-4] and most are apparently caused by viruses.[1] Social and family factors influence the incidence of illness during infancy[4-8] but documented infection rates have been less frequently studied. For this reason we examined both infection and illness during the first year of life of 131 infants followed up in the Houston Family Study between 1975 and 1980.

Materials and methods

RECRUITMENT AND MONITORING

General methods used in the Houston Family Study have been reported previously.[1-9] A total of 131 infants were observed for the first year of life from 1975 to 1980. In 1975–6 recruitment of pregnant women took place at Jefferson Davis, a county hospital; thereafter all recruiting was from the community at large at an average of two or three families a month. The infants had blood obtained at birth (cord blood) and at 4, 8, and 12 months of age. Home visits were made every week during the respiratory virus season (biweekly at other times) for history and physical examination and to obtain nasal wash specimens for virus culture from infants. Additional home or clinic visits were made as needed

for sampling of all illnesses. Diagnoses were made by a physician, nurse, or physician's assistant.

Records of all clinical contacts were available for review of illnesses. Upper respiratory illnesses (URI) were categorised as afebrile, febrile, or otitis media. For lower respiratory disease (LRD), the categories were laryngotracheobronchitis (LTB), bronchiolitis, or pneumonia. On review, illnesses lasting more than two weeks could usually be reinterpreted as two or more illnesses. When difficulty arose as to the nature or duration of an illness, the impressions of people seeing the child during the illness were used.

LABORATORY METHODS

Tissue cultures used for virus isolation were rhesus monkey kidney, MDCK, LLC-MK2, HEP-2, and WI-38.[10,11] Some specimens were inoculated into fertilised hen's eggs.[12] Serological tests included haemagglutination inhibition for influenza A and B[13] and microneutralisation for respiratory syncytial virus (RSV), parainfluenza virus types 3 (para 3),[13] and influenza A and B.[14] Fourfold rise in antibody titre (or failure of passively acquired antibody to fall) was considered evidence of infection.

SOCIAL AND FAMILY FACTORS

Personal and family data were obtained on enrolment and then recorded for each subsequent

year. Six factors were studied: sex, race, parental smoking, socioeconomic class, number of siblings, and attendance at daycare. Race was white or non-white with the latter including blacks and Mexican-Americans. An infant was considered exposed to parental smoking if either mother or father or a live-in relative smoked five or more cigarettes a day. An infant was considered a daycare attender if attendance at a daycare facility or mother's day out (sponsored by local churches) was consistent for at least five months. Finally, socioeconomic class was "low" if the family was eligible for the county hospital or made less than $12 000 a year, "medium" if the family had private medical insurance or made more than $12 000 a year, and "high" if the family had private medical insurance, made more than $12 000 a year, and one or both parents had attended at least three years of college.

ANALYSIS

Viral infection and respiratory illness rates were analysed for each family factor category. The mean number of infections or illnesses was calculated from the total number of episodes and reported as the rate per 100 child years. Chi-square analysis was done on the distribution of the data.

Results

From 1976 to 1980, 92 infants (including three sets of twins) from 75 families were followed up. There were 59 whites, 24 blacks, and nine Mexican-Americans. Forty two per cent of the black and Mexican-American families were in the low socioeconomic group compared with 15% of the white families. The 39 infants studied from spring 1975 to spring 1976 will be included in selected analyses only because of socioeconomic imbalance (38 of 39 in low socioeconomic class) and some limitation in detailed clinical information on minor or non-influenza A illnesses, or both, during this first study year. This group was composed of 13 white, 21 black, and five Mexican-American infants.

VIRUS INFECTION

The figure shows the number of infections documented for the four viruses where serology was used in addition to virus isolation. Respiratory syncytial virus (RSV) had the largest proportion of infections identified by serological methods alone (63%). Of 40 influenza A and B infections (35 type A and five type B), 40% were identified by serology alone. In addition, 42% of the parainfluenza type 3 (para 3) infections were identified by serology alone. The remainder of the infections shown in tables 1 and 2 for these four agents were identified by isolation alone or isolation plus fourfold serological rise.

Table 1 shows the virus infection according to the selected social and family factors. In general, these factors were not significantly related to rates of proved viral infection. There were, however, some interesting exceptions.

Adenovirus infection rates were significantly associated with the number of siblings and daycare attendance. Infants with one sibling had the highest rate of infection while those with no siblings had the lowest. Infants with one sibling more often attended daycare (41%) when compared with those with none or two or more sibling infants (19% and 15% respectively); this may have influenced the chi square results. Numbers became too small when further analyses of daycare by number of siblings was done for adenovirus infection so the influence of the two factors could not be separated.

Both sex and daycare attendance were significantly associated with rhinovirus infection. Girls attending daycare had a much higher rate of rhinovirus infection (169) than did boy daycare attenders (50) or all infants not in daycare (48). In addition, 54% of girl daycare attenders had multiple infections compared with 20% of the boys; 77% of girls in daycare had had at least one infection compared with 53% for all infants combined.

Seventy four per cent of low socioeconomic class infants had had at least one para 3 infection compared with 47% for medium socioeconomic class and 54% for high, and this is reflected in the trend (not significant) in overall infection rates. None of the viruses considered was significantly associated with parental smoking for 1976–80. A significant relationship was found only for RSV and smoking mothers at home ($p = 0.020$) when 1975–6 data were included.
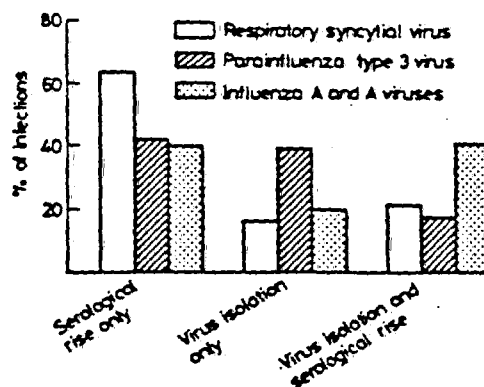
Evidence of respiratory syncytial, parainfluenza type 3, and influenza A and B virus infection in study infants, Houston Family Study 1975–80. Serological rise included failure of fall of passively acquired maternal antibody.

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Table 1 *Virus infection rates per 100 child years for 131 infants according to sex, race, smoking, Number of siblings and daycare. Houston Family Study, 1976–80.*

Table 2 *Respiratory illness rates per 100 child years for 131 infants according to sex, race, smoking, number of siblings, and daycare: Houston Family Study 1976–80.*

URI = Upper respiratory illness
LTB = Laryngotracheobronchitis
LRD = Lower respiratory disease

Table 1 shows that influenza A and B infection rates varied significantly with race. Data for 1975–6 influenza A and B infections were combined with the 1976–80 data because surveillance of the influenza A/Victoria epidemic that occurred was comparable with later years (table 3). The significant association with race was also seen in 1975–80. In addition, significant associations were found for race and influenza A only (p=0·008). Seventy three per cent of these black infants had one or more siblings (1975–80) compared with 56% of white, but for 1976–80 this was reversed (black 41% white 53%).

Table 3 *Influenza A and B infection rate per 100 child years according to selected social and family factors, 1975—80*

	No	Influenza A & B infection rate
Sex Boy	67	27
Girl	64	34
Race White	72	19
Other	59	44*
Socioeconomic class:		
Low	61	41
Medium	22	18
High	48	23
Parental smoking:		
Yes	66	33
No	65	27
No of siblings:		
0	49	18
1	41	32
>2	41	44†
Daycare:		
Yes	30	33
No	101	30

*$\chi^2=8\cdot14$, $p=0\cdot004$, influenza A only, $p=0\cdot036$ black v white, $p=0\cdot008$.
†$\chi^2=6\cdot97$, $p=0\cdot030$, influenza A only, $p=0\cdot013$ 0 v >2 $p=0\cdot008$.

Influenza A and B infection was also significantly related to number of siblings as was influenza A alone ($p=0\cdot013$). A stronger association was seen when comparing none with two or more siblings ($p=0\cdot008$). These relationships with number of siblings were not seen with the 1976—80 data only.

Independence between race and number of siblings for low socioeconomic infants was suggested by analysing all three factors simultaneously. There was a trend towards increase in the rate of infection with number of siblings for both white and non-white in the low socioeconomic group; non-white infants had higher rates compared with white in each sibling category. This was not seen in any other socioeconomic group or for the data as whole. Most influenza A and B infections (25/40), however, occurred in the low socioeconomic infants (mostly due to the A/Victoria epidemic of 1975—6) and numbers were too small in other comparisons. Regardless of how the data were grouped, all analyses comparing infants with no siblings with infants with one or two or more siblings showed lower rates of infection in those without siblings. In addition to the association with number of siblings, 70% of infants with two or more siblings had at least one school aged sibling, whereas for those with only one, the sibling tended to be of preschool age (15% school aged). During the epidemic of 1975—6, 38% of the study infants had evidence of infection and 80% of these had school age siblings.

RESPIRATORY ILLNESS

Respiratory illness rates are shown in table 2 according to the selected social and family factors. In general, the significant relationships and interesting trends found were in the area of more severe illness. As shown in the first two columns of table 2, boys had higher rates of illness in several of the diagnostic categories but none of these trends was significant. The rate of total LRD varied significantly with both socioeconomic class (low v high only) and daycare attendance, and a similar trend was noted with increasing number of siblings. There were indications that all three factors may affect total LRD independently. The larger families were distributed almost equally among all three socioeconomic classes, although low and medium classes had higher percentages of families with two or more siblings (low 39%, medium 38%, high 19%). Rates of total LRD for infants with two or more siblings were found to be highest in low socioeconomic families (166 per 100 child years) and lowest in high socioeconomic class families (80 per 100 child years). Also the low socioeconomic families were the least likely to send their infants to daycare. Only 13% of low socioeconomic infants were in daycare compared with 28% of the medium and 35% of the high socioeconomic class infants.

Rates of total LRD for girls and boys not attending daycare were 69 and 105, respectively, while girl and boy infants attending daycare had rates of 123 and 120. Rates of bronchiolitis and pneumonia were essentially equal for both sexes in daycare.

A statistically significant variation in the rate of LTB (a component of LRD) was also found in all three socioeconomic classes, but separate analysis of medium v high was found not to be significant ($p=0\cdot062$).

No statistically significant relationship was seen between total respiratory illness and parental smoking for the 1976—80 infants. Nevertheless, data on severe illnesses in 1975—6 were comparable with later years, and all six episodes of pneumonia that year occurred in infants of mothers who smoked. Overall, from 1975 to 1980 there were 11 episodes of pneumonia and nine (82%) occurred in black infants of mothers who smoked. The highest rate of pneumonia (25) was found in infants with non-employed mothers who smoked and this compared with a rate of 1·5 in those with non-employed mothers who were non-smokers ($p=0\cdot001$).

Discussion

In this study we closely monitored infants for viral infections and respiratory symptoms through the first year of life for five consecutive years. Since we studied proved viral infection regardless of illness and all illnesses regardless of severity, differences in groups based on family recognition of illness and patterns of medical care were minimised. It might therefore be expected that for such a ubiquitous group of viruses and such common illnesses the impact of family and social factors would not be impressive. In fact, we were unable to find any consistent overall relationship between respiratory viral infection or illness and the social factors studied. We had previously noted a similar lack of overall effect of breast feeding on viral respiratory infection and illness in this same population.[19] Within this general similarity of experience among infants living under different conditions, however, there were selected findings of interest, especially in relation to previous reports. This group of observations will be summarised and then discussed individually. RSV and para 3 notably could not be confidently related to any of the study factors. The infection rates of rhino, influenza, and adenoviruses were all significantly associated with two of the study factors but the strongest and clearest relationships were found for influenza viruses. Respiratory illness varied significantly with the study factors only when looking at more serious illness categories. Important trends included variation in severe illness rates with sex and number of siblings while significant relationships existed between LRD, socioeconomic class, and daycare. No differences in LRD were found in relation to parental smoking as an isolated factor.

RSV is a major cause of respiratory illness in young children, especially bronchiolitis and pneumonia.[12 18] Previous studies have found no correlation between RSV infection and sex, race, or socioeconomic class[17–19] although sex, low socioeconomic class, and number of siblings, may influence the outcome of infection.[16 20 21] Our data also show no correlation between RSV infection and sex, race, or socioeconomic class, and, in addition, we found no association with daycare. The relationship to parental smoking must be considered questionable because of the limitations of the data relative to this virus in 1975–6. Hall *et al* also found a questionable relationship between parental smoking and RSV infection so that any association continues to be undocumented.[22] Sixty nine per cent of our study infants had had at least one RSV infection; this shows the high incidence in this age group.

Parainfluenza type 3 virus is also a major cause of LTB in young children and is an important cause of

bronchiolitis and pneumonia in infants and children,[19] but the influence of social and family factors have been little studied. Our results show a higher incidence of initial infections among infants of low socioeconomic class but no significant association with any of the factors studied. Fifty five per cent of the infants had had at least one parainfluenza 3 virus infection.

Our study indicates that for influenza viruses (particularly type A) both race and number of siblings influence the rate of infection. Kim *et al* found that a larger percentage of black infants (especially boys) in hospital for respiratory illness during 11 influenza epidemics had influenza A virus infection,[23] and our very different approach also gave indications that blacks are at a greater risk for influenza A infection. The effect of race on influenza infection was not influenced by family size or socioeconomic class even though a larger number of non-whites were in the low socioeconomic class. The present data also point to older siblings, particularly school age children, as introducers; infants were more likely to be infected if they had school aged siblings in the home. This was especially true during the epidemic of 1975–6 as previously reported[7] and has been observed by others.[24] Hall *et al* found that preschoolers were more often responsible for spread of infection within the family based on age-specific infection rates, but they noted that infection rates based on a fourfold serological rise rather than the twofold rise they used would have shifted the highest age-specific infection rates to school age children.[25]

Rhinovirus infection rates were found to be influenced by sex and daycare attendance. In both instances the reason appeared to be a high rate of infection in girls attending daycare for which we have no explanation.

Variation in illness with social and family factors was generally restricted to LRD rates and most of the findings reported previously also refer to LRD. Boys have been shown to have higher rates of LRD compared with girls[1 18 19] at least to the age of 6. Although we found that the difference between boys and girls was not significant for LRD, the ratio of illness, especially when looking only at non-daycare attenders, was very close to the 60:40 ratio found by Gardner.[3] The presence of siblings has also been shown by previous studies to affect the seriousness and number of illnesses.[1 18] We were unable to show that the difference in illness rates between number of siblings was significant for LRD but the trend was very suggestive.

Low socioeconomic status has been thought to influence the rate of respiratory illness by means of overcrowding, large family size, and inadequate medical care.[4 20] We provided uniform medical care

and still found a higher rate of LRD among infants of low socioeconomic class even when controlled for family size (although numbers were small) and despite the fact that few of these infants were in daycare. Factors other than medical care or family size seem to be important influences on the incidence of LRD in the low socioeconomic infants. Trends to more infection and illness in general were present in this group.

Past studies have implicated daycare attendance as a cause of increased respiratory illness in children, especially infants. Strangert and Loda *et al* noted this in infants aged 6–15 months and under 12 months old, respectively.[17][18] Vihma found annual illness rates in daycare compared with home to be 6·3 v 2·5.[19] These results are in agreement with our findings. In addition, we found that girl infants in daycare seem to lose the relative "protection" from LRD observed for girl infants at home. Rates of serious lower respiratory disease—that is, bronchiolitis and pneumonia—wer equal in boy and girl daycare attenders.

Infants of parents who smoked in our study were not at greater risk for viral infection or respiratory illness and even had a lower rate of LTB. The only exception to this was a significant relationship between pneumonia and parental smoking (especially mothers at home who smoked) only evident when the 1975–6 data were included. This effect could not be separated from the influence of race or socioeconomic class. Our observations are in contrast with those of Harlap and Davies[20] and Leeder *et al*.[5] Both studies found a highly significant relationship between passive smoking and lower respiratory illness, specifically bronchitis and pneumonia. Methods in these studies differed considerably from our own; Harlap and Davies used data from large numbers of infants in hospital whereas Leeder *et al* followed up a cohort of children by means of yearly questionaires. Although the total number of episodes of LRD (112 including 1975) experienced by the infants in our study was small by comparison (especially pneumonia), ascertainment was more direct and illnesses were well documented.

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Ware, J.H., Dockery, D.W., Spiro, A., Speizer, F.E., Ferris, B.G.
"Passive Smoking, Gas Cooking, and Respiratory Health of Children
Living in Six Cities" American Review of Respiratory Disease 129:
366-374, 1984.

SUMMARY: As part of a longitudinal study of the respiratory health
effects of indoor and outdoor air pollutants, pulmonary function,
respiratory illness history, and symptom history were recorded at
2 successive annual examinations of 10,106 white children living
in 6 cities in the United States. Parental education, illness
history, and smoking habits also were recorded, along with the
fuel used for cooking in the child's home. Maternal cigarette
smoking was associated with increases of 20 to 35% in the rates
of 8 respiratory illnesses and symptoms investigated, and paternal
smoking was associated with smaller but still substantial increases.
Illness and symptom rates were linearly related to the number of
cigarettes smoked by the child's mother. Illness rates were higher
for children of current smokers than for children of ex-smokers.
The associations between maternal smoking status and childhood
respiratory illness and symptoms were reduced but not eliminated
by adjustment for parental illness history. Levels of forced
expiratory volume in one second (FEV_1) were significantly lower
for children of current smokers than for children of nonsmokers
at both examinations and highest for children of ex-smokers. Levels
of forced vital capacity (FVC) were lower for children of nonsmokers
than for children of current smokers at both examinations, but the
difference was statistically significant only at the first
examination. Both the increase in mean FVC and the decrease in
mean FEV_1 among children of current smokers were linearly related
to daily cigarette consumption. None of the respiratory illnesses
and symptoms studied was significantly associated with exposure to
gas cooking in the child's home. The largest odds ratio for
respiratory illness before 2 yr of age was 1.13 ($p = 0.07$).
Exposure to gas stoves was associated with reductions of 0.7% in
mean FEV_1 and 0.6% in mean FVC at the first examination ($p < 0.01$)
and reductions in both measures of 0.3% at the second examinations
(NS). The estimated effect of exposure to gas stoves was reduced
by approximately 30% after adjustment for parental education. These
results provide strong support for a causal effect of sidestream
cigarette smoke on increased respiratory illness and reduced FEV_1
values in preadolescent children. They also suggest that exposure
to gas stoves may be associated with reduced pulmonary function
but do not show increases in respiratory illness among children
exposed to gas stoves. Understanding of the health effects of
these indoor pollutants will be improved by studies quantifying
individual exposure to cigarette smoke and gas stove combustion
products.

Passive Smoking, Gas Cooking, and Respiratory Health of Children Living in Six Cities[1-3]

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Introduction

Acute illness resulting from exposure to high concentrations of indoor air pollutants is a well-recognized clinical entity. Tragic episodes arising from suicide attempts or accidents with carbon monoxide are too common to require detailed documentation. Far more difficult to assess are the health effects of indoor exposures to the concentrations of gases and particles encountered in the usual activities of daily living.

Because most people spend more than 80% of their time indoors (1,2), and because efforts to reduce air exchanges in homes have increased in the last several years, it is important to determine whether air contaminants from indoor sources affect respiratory illness rates and pulmonary function levels in children and adults. Respirable particulate concentrations are higher in homes of smokers than in homes of nonsmokers (3, 4), and increased concentrations of nitrogen dioxide (NO_2) are found in homes where gas is used for cooking (5-9). However, the respiratory health effects of exposure to sidestream cigarette smoke and gas combustion products have only recently been investigated.

Most studies of children exposed to cigarette smoke have found increases in respiratory illnesses and symptoms (10-16) and reductions in indexes of pulmonary function (11-17), although a few studies have failed to find one or both of these associations (10, 18, 19). Several studies have found increased respiratory illness and symptom prevalence in homes with gas stoves (10, 20-22), but the associations have often been weak, and other studies have found no significant associations (23-25). Most studies of gas cooking and pulmonary function levels have found no association (10, 22, 23), although Hasselblad and associates (26) reported reduced FEV_1 among older girls living in homes with gas stoves. Thus, the literature indicates reasonably good agreement about the health significance of passive smoking but is inconsistent regarding the effects of gas stoves.

The Six-Cities Study of the Health Effects of Respirable Particulates and Sulfur Dioxide (27) is a longitudinal study of the respiratory health effects of air pollutants among children and adults living in 6 cities in the United States. Although the study is longitudinal, completion of the first 2 annual visits by participating children permits a cross-sectional analysis of the effects of stove type and parental smoking habits on pulmonary function, respiratory illnesses, and symptoms at enrollment and the first follow-up visit. These results update previous reports on gas stove exposure and passive smoking from this study (28, 29). The previous reports presented preliminary analyses from data provided by 8,120 white children from 6 to 10 yr of age and indicated increased respiratory illness before 2 yr of age and decreased pulmonary function levels in children

SUMMARY As part of a longitudinal study of the respiratory health effects of indoor and outdoor air pollutants, pulmonary function, respiratory illness history, and symptom history were recorded at 2 successive annual examinations of 10,106 white children living in 6 cities in the United States. Parental education, illness history, and smoking habits also were recorded, along with the fuel used for cooking in the child's home. Maternal cigarette smoking was associated with increases of 20 to 35% in the rates of 6 respiratory illness and symptom measures, and paternal smoking was associated with smaller but still substantial increases. Illness and symptom rates were linearly related to the number of cigarettes smoked by the child's mother. Illness rates were higher for children of current smokers than for children of ex-smokers. The associations between maternal smoking status and childhood respiratory illnesses and symptoms were reduced but not eliminated by adjustment for parental illness history. Levels of forced expiratory volume in 1 second (FEV_1) were significantly lower for children of current smokers than for children of nonsmokers at both examinations and highest for children of ex-smokers. Levels of forced vital capacity (FVC) were lower for children of nonsmokers than for children of current smokers at both examinations, but the difference was statistically significant only at the first examination. Both the increase in mean FVC and the decrease in mean FEV_1 among children of current smokers, and their variation in daily cigarette consumption, were consistent with the hypothesis that exposure to maternal smoke depresses small-airway function. Respiratory illness before 2 yr of age was significantly associated with exposure to gas cooking in the child's home. The largest odds ratio for respiratory illness before 2 yr of age was 1.13 (p = 0.07). Exposure to gas stoves was associated with reductions of 0.7% in mean FEV_1 and 0.8% in mean FVC at the first examination (p < 0.01) and reductions in both measures of 0.3% at the second examinations (NS). The estimated effect of exposure to gas stoves was reduced by approximately 30% after adjustment for parental education. These results provide strong evidence for an effect of passive cigarette smoke on increased respiratory illness and reduced FEV_1 values in preadolescent children. They also suggest that exposure to gas stoves may be associated with reduced pulmonary function but do not show increases in respiratory illness among children exposed to gas stoves. Understanding of the health effects of these indoor pollutants will be improved by studies quantifying individual exposure to cigarette smoke and gas stove combustion products. AM REV RESPIR DIS 1984; 129:366-374

exposed to gas stoves. Parental smoking was found to be associated with increased respiratory illness but not with pulmonary function levels. This report presents a reassessment of those associations in the complete study cohort of 10,106 white children, using recently reported normal values in the pulmonary function analyses (30). We provide evidence for an exposure-response relationship between the amount of maternal cigarette smoking and indexes of respiratory health. We also examine the importance of parental respiratory illness and socioeconomic status as predictors of illness in children.

Methods

Study Population

The six cities were selected to represent a range of air quality based on their historic levels of outdoor pollution. Cooperation of local school authorities was required, and the school districts selected had to be of manageable size. The 6 communities included Watertown, Massachusetts; Kingston and Harriman, Tennessee; a geographically defined area in the southeast section of St. Louis, Missouri; Steubenville and Mingo Junction, Ohio; Portage, Wisconsin and surrounding towns; and a random sample of 50% of the schools in Topeka, Kansas.

In each city, the initial examinations included all first- and second-grade school children in both the public and private schools within the community. Because Portage was considerably smaller than the other districts, the initial examination included children up to the fifth grade. In each year after the initial examination, the same children were seen again and a new first grade was added until approximately 1,500 children were enrolled in each community. All available children in each community are reexamined annually. The population for this analysis is made up of all white children enrolled during the first 3 visits to each city. Nonwhite children were excluded from this analysis because the other racial and ethnic groups were relatively small.

Health, Exposure, and Demographic Information

At each visit, a questionnaire was sent home (with an explanatory letter) to be completed by a parent or guardian and returned to the school. Families reported the number of persons living in the home and their smoking habits, parental occupation and educational background, and the fuels used for cooking and heating. Information regarding respiratory illnesses and symptoms was requested in a format similar to that recommended by the Epidemiology Standardization Project (31). Although children in the fourth and higher grades were asked separately about their smoking habits, smoking was rare in the young children included in this analysis, and was not considered as a possible risk factor.

The children were examined at school. Their weight and standing height in stocking feet were measured, and they performed forced expiratory maneuvers on a recording spirometer (Stead-Wells survey spirometer; Warren E. Collins, Braintree, MA) while sitting with free mobility and without a nose-clip. Each child performed at least 5 forced expirations but not more than 8. Forced vital capacity (FVC) and forced expiratory volume in one second (FEV_1) were measured from the acceptable blows determined by the tester. The mean of the best 3 efforts was calculated, corrected to body temperature and water saturation. Detailed description of measurement procedures is given elsewhere (30).

Of the respiratory illnesses and symptoms surveyed at the initial visit, responses concerning history of bronchitis, doctor-diagnosed respiratory illness before 2 yr of age, and respiratory illness in the previous year that kept the child at home 3 days or more were analyzed. From the questionnaire given at the first follow-up visit 1 yr later, the frequency of respiratory illness in the previous year that kept the child at home 3 days or more, bronchitis in the previous year, and the prevalence of persistent cough (for 3 months of the year or more) and persistent wheeze (most days or nights or apart from colds) were analyzed. An index of lower respiratory illness, indicating the presence of either bronchitis, respiratory illness, or persistent cough during the past year, was also computed and analyzed.

Pulmonary function values were transformed to their logarithms (see Statistical Methods) and then expressed as residuals (differences) from height, weight, age, and sex-specific expected values based on previously reported prediction equations (30). Pulmonary function residuals from the initial and first follow-up visits were investigated for associations with exposure to gas stoves and sidestream cigarette smoke. Results of these analyses are reported as deviations from 100% of the ratio of observed to expected pulmonary function level.

Parental smoking status was expressed both as a three-level variable based on reported smoking history (never smoked, ex-smoker, and current smoker) and as an ordinal variable, coded as the reported number of cigarettes currently smoked per day by each parent. To determine a dichotomous variable for cooking fuel, homes using any gas for cooking were classified as gas homes. A positive history of parental respiratory illness was defined as a history of bronchitis, emphysema, or asthma for either parent. To adjust for the effect of socioeconomic factors on respiratory health, we defined 3 classes based on the mean number of years of schooling of the parents (< 9, 9-12, > 12). For children in single-parent households, the years of education of that parent were used. As an alternative measure of socioeconomic status, we considered an index proposed by Green (32) based on education and occupation.

Statistical Methods

The illness and symptom outcomes were analyzed by multiple logistic regression (33, 34), using BMDP (35). For each outcome, a regression model was constructed, including gas cooking and parental smoking variables (because of their a priori interest as risk factors), and other confounding variables as identified by prior analyses. Statistical significance of regression coefficients was determined by the chi-square approximation for the likelihood ratio statistic. Independent variables considered included maternal and paternal smoking status, stove type, heating fuel, air conditioning, and parental education. Because heating fuel and air conditioning did not enter significantly into any regression model, these variables are not discussed further. City-cohort, an 18-category variable designating the city and year of enrollment, was included in every model to eliminate possible confounding effects caused by city of residence and entry cohort. Parental respiratory illness history was then added to the explanatory model to assess its importance as an intermediate or explanatory variable. The logistic regression analysis gave a regression coefficient and standard error for each exposure variable. These coefficients were reexpressed as point estimates and 95% confidence intervals for the relative odds of disease for exposed relative to unexposed children. The adequacy of these summaries was examined by graphic and tabular inspection of the illness and symptom rates for groups of children defined by values of the independent variables. Directly standardized rates, based on the entire sample as the reference population, were used to summarize illness and symptom rates in different exposure groups. To avoid empty cells, the rates given in table 4 are standardized for city rather than city-cohort.

We have previously reported (30) that for preadolescent children, FVC and FEV_1 should be expressed on the logarithmic scale to quantify variability as a percentage of the expected pulmonary function level. That report gave expected values for the logarithm of FEV_1, $ln(FEV_1)$, and of $ln(FVC)$, based on a linear regression of observed values on sex and the logarithms of height, weight, and age. For this analysis, residuals were defined for each child by the difference between the logarithms of the observed and expected values of FEV_1 and FVC (or equivalently, the logarithm of the ratio of observed to expected). These residuals were investigated further by multiple regression analysis. For each visit and each pulmonary function outcome, an explana-

TABLE 1

NUMBER OF WHITE CHILDREN SEEN BY CITY AND SCHOOL YEAR AT THE INITIAL EXAMINATION, AND TOTAL NUMBER OF WHITE CHILDREN REEXAMINED APPROXIMATELY ONE YEAR LATER

City	Season	First Examination						Second Examination (total)
		74-75	75-76	76-77	77-78	78-79	Total	
Watertown	Fall	613	384	387			1,384	1,197
Kingston	Spring	533	345	378			1,256	1,030
St. Louis	Fall		1,171	749	197		2,117	1,856
Steubenville	Spring		824	475	479		1,778	1,559
Portage	Fall			701	656	320	1,677	1,493
Topeka	Spring			1,412	275	207	1,894	1,449
Total							10,106	8,384

tory model was constructed by an approach parallel to that described previously for analysis of respiratory illnesses and symptoms. To express the results as percentage change, we computed the antilogarithm of each regression coefficient, and multiplied by 100. Thus, associations between outcomes and indirect exposure measures are expressed as change from 100% in the ratio of observed to expected FEV_1 or FVC associated with a change in exposure status, along with 95% confidence intervals or approximate standard errors derived from the analysis on the logarithmic scale. Results are given from the first 2 annual spirometric examinations of participating children.

Results

Sample

During the first 3 visits to the 6 cities, 11,048 white children entered the study. Analyses for this report were restricted to the 10,106 children 6 to 9 yr of age at enrollment (table 1). At the first follow-up visit, 8,380 (83%) of these children were reexamined. Reexamination rates varied from a low of 77% in Topeka, where follow-up was affected by school closings, to a high of 89% in Portage. Sample sizes for individual symptom, illness, and pulmonary function analyses varied because of missing data, particularly for respiratory illness before 2 yr of age, which was not include in the questionnaire used during th first visit to Watertown and Kingston Harriman.

Of the 10,106 children, 1,107 (11.0% did not have acceptable spirometri data. The frequency of unacceptabl spirometic tests was strongly related to age of the child. The rate for those 6 yr of age was 15.2%; for those 7 yr of age 9.6%; for those 8 yr of age, 7.4%; for those 9 yr of age, only 5.6%. At the first follow-up visit, the overall frequency of unacceptable tracings dropped to 5.7%. There was no association of unacceptable lung function examinations with any reported respiratory illness or symptom after controlling for age and examination.

Demographic Variables, Family History, and Respiratory Health

Boys had uniformly higher illness and symptom rates than did girls (table 2). All respiratory illnesses and symptoms, except history of bronchitis, were reported more frequently for younger than for older children. The negative association between illness before the age of 2 and age suggests that parents

TABLE 2

FREQUENCY (RATE PER 1,000) OF REPORTED ILLNESSES AND SYMPTOMS, BY SEX, AGE, CITY, PARENTAL EDUCATION, AND REPORTED PARENTAL RESPIRATORY ILLNESS HISTORY, DIRECTLY STANDARDIZED FOR SEX, AGE, AND CITY

	1st Examination			2nd Examination				
	Doctor-Diagnosed Illness before age 2	History of Bronchitis	Respiratory Illness Last Year	Respiratory Illness Last Year	Bronchitis	Cough	Wheeze	Lower Respiratory Index
Number	9,004	10,008	9,994	8,292	8,288	8,264	8,237	8,240
Sex								
Boys	241	163	140	148	89	95	127	237
Girls	191	138	134	137	80	84	102	219
Age								
6	227	155	144	-	-	-	-	-
7	212	148	140	148	92	99	121	239
8	222	151	124	144	78	88	113	228
9	183	153	108	129	81	87	120	213
10	-	-	-	121	77	87	92	194
City								
Portage	223	141	89	87	45	71	111	147
Topeka	208	134	125	155	82	74	115	224
Watertown	129	113	139	156	56	62	89	216
Kingston	341	195	181	218	128	105	148	313
St. Louis	196	127	126	94	80	106	111	204
Steubenville	221	210	171	168	117	119	125	281
Parent's Education								
<High school	265	145	152	133	87	115	146	236
High school	220	150	137	141	82	90	118	225
>High school	195	157	130	145	86	82	94	228
Parent's Illness								
No	174	116	109	112	62	75	91	184
Yes	299	261	207	197	158	138	184	330

* Excludes forty-four 7-yr-old and nine 11-yr-old children at the second examination.

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are less likely to recall early illnesses as the child matures. Rates varied substantially among cities, typically being highest in Kingston and Steubenville. Rates also varied within city from year to year (not shown). Thus, further analyses were adjusted for sex, age, and city-cohort. Illness before 2 yr of age, cough, wheeze, and respiratory illness at the initial examination were negatively associated with level of parental education (table 2). For the other 4 outcomes, the association was either absent or weakly positive. The effect on risk factor analyses of controlling for education or other measures of socioeconomic status is discussed below.

The strongest risk factor for respiratory illness among these children was a history of parental respiratory illness (table 2). Children whose parents had a positive history had 72 to 155% higher illness and symptom rates than did children whose parents had a negative history. Because parental history could be either an intermediate or a confounding variable for the effects of gas cooking and sidestream cigarette smoke, analyses of these risk factors are presented both with and without adjustment for family illness history.

Individual values of $\ln$ FVC and $\ln$ FEV_1 were adjusted for sex and age by subtracting the sex-, age-, height-, and

weight-specific predicted values from each observation (30). Consequently, mean residuals of FVC and FEV_1 (expressed in percent) were not significantly associated with either sex or age (table 3). Pulmonary function residuals were smaller at the first than at the second examination for both boys and girls. This was due primarily to poor performance of the spirometric maneuver at the first examination. Mean residuals differed significantly among the cities. The city-specific means are similar at the 2 examinations for 4 of the 6 cities. Topeka and St. Louis show significant increases between the first and second examinations. Thus, further analyses of the effects on pulmonary function level of exposure to gas cooking and parental smoking were adjusted for city-cohort.

Although adjusted mean residuals of FVC and FEV_1 increase with level of parental education (table 3), neither association is significant. Parental respiratory illness history is not significantly associated with either FVC or FEV_1.

Parental Smoking

When children were classified by maternal smoking status, children of nonsmokers had the lowest illness or symptom rate, children of current smokers

the highest rate, and children of ex-smokers had an intermediate rate. For all 8 illnesses and symptoms studied (table 4) the rates for the 3 exposure groups were significantly different ($p < 0.01$) in every instance. The same general pattern was observed when children were classified by paternal smoking status, but with occasional exceptions, and the differences between exposure groups were not uniformly significant. Thus maternal smoking status was a consistently stronger risk factor than paternal smoking status. When current maternal and paternal smoking status were considered simultaneously, children of 2 smoking parents were at highest risk for each outcome except bronchitis in the previous winter (table 4). Results of logistic regressions were consistent with an additive effect of the number of smoking parents on the risk of illness.

Illness and symptom rates had a strong linear relationship on the logistic scale with level of maternal smoking measured as the reported current daily cigarette smoking by the child's mother (table 5). (Ex-smokers were excluded from this analysis.) The linear association was highly significant ($p < 0.001$) for every outcome except bronchitis for the last year ($p < 0.01$) and respiratory illness in the previous year at the first examination ($p = 0.09$). A nonlinear component for these relationships could not be identified for any illness or symptom. Linear relationships were also found when the analysis was restricted to children of housewives, and when the combined current daily cigarette smoking of the father and mother was used to estimate level of exposure. However, the comparisons with maternal smoking level produced the strongest associations.

A reported parental history of bronchitis, emphysema, or asthma was a highly significant independent risk factor for each of the illnesses and symptoms studied (table 6). Odds ratios for the 8 outcomes by parental history varied from 1.99 to 2.88. Adjustment for parental respiratory illness history reduced the estimated effects of maternal smoking on respiratory illnesses and symptoms, but the associations remained positive and in 5 of the 8 outcomes considered, statistically significant.

Adjustment for the educational attainment of the parents reduced only slightly the estimated effects of mater-

TABLE 3

MEAN RESIDUAL PULMONARY FUNCTION (%)* AT FIRST (n = 8,994) AND SECOND EXAMINATIONS (n = 7,145) BY SEX, AGE, CITY, PARENTAL EDUCATION, AND REPORTED PARENTAL ILLNESS HISTORY

	1st Examination		2nd Examination	
	FVC	FEV_1	FVC	FEV_1
Sex				
Boys	-0.35	-0.18	+1.21	+0.80
Girls	-0.24	-0.12	+1.01	+0.80
Age				
6	-0.38	+0.03		
7	-0.47	-0.27	+1.01	+0.77
8	-0.28	-0.26	+1.01	+0.93
9	+0.72	-0.06	+1.01	+0.57
10			+0.92	+0.89
City				
Portage	+2.70	+2.14	+2.87	+2.57
Topeka	-1.81	-1.73	+2.30	+1.54
Watertown	-1.94	-0.95	-2.00	-0.59
Kingston	+0.22	-0.92	+0.64	-0.40
St. Louis	-0.66	-0.34	+1.36	+0.90
Steubenville	+0.42	+0.81	+0.66	+0.23
Parent's Education				
<High school	-0.41	-0.54	-0.23	-0.44
High school	-0.13	-0.14	-0.13	-0.17
>High school	+0.38	+0.45	+0.39	+0.52
Parent's Illness				
No	+0.02	+0.24	+0.02	+0.13
Yes	+0.23	-0.27	+0.21	-0.23

Definitions of abbreviations: FVC = forced vital capacity; FEV_1 = forced expiratory volume in one second.
* Expressed as change from 100% in ratio of observed to expected value.

TABLE 4

FREQUENCY (RATE PER 1,000) OF REPORTED ILLNESSES AND SYMPTOMS (AND STANDARD ERRORS) BY PARENTAL SMOKING AND STOVE TYPE, DIRECTLY STANDARDIZED FOR AGE, SEX, AND CITY

	1st Examination				2nd Examination				
	Number at 1st Examination	Doctor-Diagnosed Illness before age 2	History of Bronchitis	Respiratory Illness Last Year	Respiratory Illness Last Year	Bronchitis	Cough	Wheeze	Low Res; ratio Inde
Smoking Status									
Mother									
Never	4,044	193 (6)	137 (5)	124 (5)	130 (6)	74 (4)	78 (5)	99 (5)	205 (
Ex	1,485	205 (11)	152 (9)	131 (9)	147 (10)	78 (7)	93 (8)	114 (9)	239 (
Current	4,208	242 (7)	159 (6)	149 (5)	150 (6)	95 (5)	98 (5)	128 (6)	243 (
Unknown	372								
Father									
Never	1,832	185 (10)	135 (8)	129 (8)	127 (9)	79 (7)	78 (7)	104 (8)	202 (1
Ex	1,784	204 (10)	160 (9)	123 (8)	138 (8)	89 (7)	79 (7)	106 (8)	222 (1
Current	5,171	229 (6)	149 (5)	137 (5)	143 (5)	82 (4)	97 (5)	119 (5)	231 (
Unknown	1,319								
Current Parental									
Neither	2,726	173 (12)*	130 (10)*	123 (6)	129 (7)	76 (5)	77 (6)	99 (6)	206 (1
Father Only	2,193	203 (8)	141 (7)	130 (7)	134 (8)	73 (6)	87 (6)	107 (7)	217 (1
Mother Only	817	209 (17)	151 (15)	137 (12)	144 (13)	100 (11)	76 (10)	117 (12)	227 (1
Both	2,792	235 (7)	160 (6)	143 (7)	148 (8)	90 (6)	106 (7)	131 (7)	240 (5
Unknown	1,578								
Stove Type									
Gas	4,685	216 (8)	140 (7)	146 (7)	135 (8)	88 (7)	88 (6)	126 (9)	235 (1
Electric	5,035	204 (7)	161 (6)	135 (6)	144 (6)	86 (5)	88 (5)	116 (6)	222 (7
Unknown	388								

* Based on smoking history rather than on current smoking.

nal smoking on respiratory illness and symptoms; however, in all cases, a statistically significant positive relationship remained. In particular, for wheeze, which had the strongest association with parental education (table 2), the estimated odds ratio for exposure to maternal smoking of 1 pack per day relative to no exposure was 1.30 (95% confidence interval, 1.15 to 1.47), when adjusted for parental education, versus 1.34 (1.19 to 1.47) without adjustment.

The χ^2 test for linear trend was 17.86 ($p < 0.0001$) after adjustment for parental education. A similar result was obtained using Green's index of socioeconomic status (32).

The FVC was significantly higher for children of mothers who were either current or ex-smokers, relative to children of nonsmokers, at the first examination ($p < 0.05$) (table 7). A nonsignificant association in the same direction was observed at the second examina-

tion. A similar pattern was observe based on the father's smoking. Children whose mothers were current smokers had 0.6% lower mean FE than children of nonsmokers at the first examination ($p = 0.03$) and 0.9% lower mean level at the second examination ($p < 0.001$). Children of ex-smoking mothers had the largest FEV, residual at both examinations. The difference between the ex-smoking and current smoking groups were significant ($p < 0.05$), whereas those between the ex smoking and nonsmoking groups were not. Children whose fathers were current smokers had a reduction in FEV of 0.01% at the first examination (NS and 0.7% at the second ($p = 0.03$) relative to children of nonsmokers. Among current smokers, maternal smoking was more strongly associated with reduced FEV, than was paternal smoking when the two exposures were considered jointly (table 7).

Current maternal smoking level was significantly linearly associated with increased FVC ($p = 0.006$) only at the first examination. A highly significant negative association ($p < 0.001$) between maternal smoking level and FEV, was found at both examinations (figure 1). If a child's mother smoked 1 pack of cigarettes per day, the estimated reduction in the child's FEV, was 0.7 ± 0.2% at the first examina-

TABLE 5

RELATIVE ODDS OF RESPIRATORY ILLNESSES AND SYMPTOMS BY MOTHERS' REPORTED DAILY SMOKING, COMPARED WITH CHILDREN WHOSE MOTHERS REPORTED NEVER SMOKING

		Maternal Smoking Current Daily Smoking							Linear Trend	
	Number	0	1-5	6-15	16-25	26-35	36-45	46 +	χ^2	p
Doctor-Diagnosed respiratory illness before age 2	7,273	1.00	1.04	1.09	1.42	1.48	1.58	2.69	41.88	0.0000
History of bronchitis	7,944	1.00	1.03	1.19	1.20	1.42	1.26	2.04	13.66	0.0002
Respiratory illness last year (1st exam)	7,507	1.00	1.58	.97	1.15	1.56	1.01	1.07	2.95	0.086
Respiratory illness last year (2nd exam)	6,613	1.00	1.06	1.07	1.15	1.42	1.84	1.26	13.13	0.0003
Bronchitis last year	6,613	1.00	1.74	1.24	1.25	1.08	1.63	1.58	6.34	0.012
Cough last year	8,594	1.00	1.01	1.30	1.11	1.46	2.12	1.24	14.52	0.0001
Wheeze last year	8,578	1.00	1.17	1.11	1.27	1.39	2.31	1.35	24.94	0.0000
Lower respiratory index	8,578	1.00	1.15	1.09	1.20	1.29	1.78	1.87	23.82	0.0000

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TABLE 6

ODDS RATIOS FOR RESPIRATORY ILLNESSES AND SYMPTOMS BY REPORTED PRESENCE OF RESPIRATORY ILLNESS IN PARENTS AND MOTHERS' SMOKING 1 PACK/DAY, WITH AND WITHOUT ADJUSTMENT FOR PARENTAL RESPIRATORY ILLNESS HISTORY. ALL ANALYSES ARE CONTROLLED FOR AGE, SEX, AND CITY-COHORT

	Number	Parents' Illness Only	Mothers' Smoking Only	Mothers' Smoking Controlled for Parent's Illness
Doctor-diagnosed respiratory illness before age 2	6,676	2.05*	1.35*	1.28*
History of bronchitis	6,675	2.77*	1.16*	1.07
Respiratory illness last year (1st exam)	6,679	2.16*	1.25*	1.18*
Respiratory illness last year (2nd exam)	5,414	1.99*	1.15†	1.09
Bronchitis	5,416	2.88*	1.19†	1.08
Cough	5,401	2.11*	1.34*	1.26*
Wheeze	5,385	2.30*	1.31*	1.23*
Lower respiratory index	5,390	2.32*	1.23*	1.16‡

* $p < 0.001$.
† $p < 0.05$.
‡ $p < 0.01$.

tion and $0.8 \pm 0.2\%$ at the second examination. Adjustment for parental education did not change appreciably the estimated effect of smoking on FVC or FEV_1.

Because of the positive association between passive smoke exposure and respiratory illnesses and symptoms in these children, the regression analyses of FVC and FEV_1 were repeated, controlling for each of the illnesses and symptoms. There was no significant association between FVC or FEV_1 and any of the respiratory illnesses or symptoms in the previous year. The FEV_1 was significantly reduced for children with a reported history of bronchitis or respiratory illness before 2 yr of age, -1.5% at the first examination ($p < 0.001$) and -1.3% at the second exami-

nation ($p < 0.001$). The FVC was also reduced by -0.5 and -0.2%, but the differences were not significant. Controlling for such a history did not substantially change the estimated effect of maternal smoking. For example, the estimated reduction in FEV_1 associated with maternal smoking of 1 pack per day, controlling for history of respiratory illness, was $0.7 \pm 0.2\%$ at both examinations (table 7).

To investigate the possibility of differential effects of parental smoking on boys and girls, the analysis of each pulmonary function and respiratory illness outcome was repeated separately for boys and girls, using maternal smoking level as the risk factor. For the 8 respiratory illness and symptom outcomes, the estimated effect of maternal smok-

ing was larger in boys in 5 instances and larger in girls in 3 instances (results not shown). The difference in the odds ratios was not statistically significant for any of the 8 outcomes. Similarly, the estimated reduction in FEV_1 associated with maternal cigarette smoking did not differ significantly for boys and girls.

Gas Cooking

Directly standardized rates of reported illnesses and symptoms (table 4) failed to show a consistent pattern of increased risk for children from homes with gas stoves compared with children from homes with electric stoves. Logistic analyses (not shown) controlling for age, sex, city-cohort, and maternal smoking level gave estimated odds ratios for the effect of gas stoves ranging between 0.93 and 1.07 for bronchitis, cough, wheeze, lower respiratory index, and illness for the last year reported at either examination. None of these odds

TABLE 7

MEAN RESIDUAL PULMONARY FUNCTION LEVEL* (AND STANDARD ERROR) BY SMOKING STATUS AND TYPE OF COOKING STOVE, ADJUSTED FOR CITY-COHORT

	1st Examination		2nd Examination	
	FVC	FEV_1	FVC	FEV_1
	%	%	%	%
Smoking Status				
Mother				
Never	−0.40 (0.21)	+0.17 (0.19)	−0.14 (0.21)	+0.37 (0.19)
Ex	+0.55 (0.33)	+0.84 (0.31)	+0.26 (0.33)	+0.42 (0.31)
Current	+0.14 (0.19)	−0.48 (0.18)	+0.02 (0.21)	−0.53 (0.20)
Father				
Never	−0.45 (0.30)	−0.05 (0.29)	+0.24 (0.30)	+0.57 (0.29)
Ex	+0.41 (0.30)	+0.86 (0.28)	+0.03 (0.28)	+0.41 (0.27)
Current	+0.07 (0.18)	−0.06 (0.17)	−0.01 (0.19)	−0.13 (0.18)
Current parental				
Neither	−0.75 (0.37)	−0.17 (0.36)	+0.33 (0.38)	+0.83 (0.35)
Father only	+0.11 (0.27)	+0.61 (0.26)	−0.13 (0.28)	+0.18 (0.26)
Mother only	+0.38 (0.45)	−0.09 (0.43)	−0.40 (0.43)	−0.72 (0.44)
Both	+0.01 (0.25)	−0.85 (0.24)	+0.08 (0.26)	−0.41 (0.25)
Stove type				
Electric	+0.33 (0.18)	+0.36 (0.17)	+0.16 (0.18)	+0.14 (0.17)
Gas	−0.32 (0.19)	−0.33 (0.18)	−0.16 (0.19)	−0.14 (0.19)

For definitions of abbreviations, see table 1.
* Expressed as change from 100% in ratio of observed to expected value.
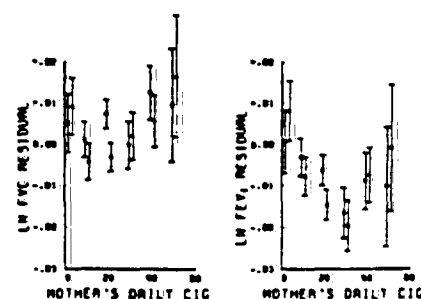
Fig. 1. Mean ln pulmonary function residuals ($\pm$ 1 SD) by mothers' reported daily cigarette smoking, compared with children whose mothers have never smoked. Squares represent the first examination (n = 7,112) and triangles represent the second examination (n = 6,278).

ratios was significantly different from 1. Only the odds ratios (OR) for history of bronchitis (OR = 0.86; 95% confidence interval, 0.74 to 1.00) and respiratory illness before the age of 2 (OR = 1.13; 95% confidence interval, 0.99 to 1.28) approached statistical significance.

Use of gas stoves was strongly associated with parental educational attainment. The percentage of homes using gas stoves was 65% for families in the group with lowest education, 46% in the middle group, and 33% in the highest. When the logistic analysis was repeated with adjustment for parental education, the estimated odds ratio for illness before 2 yr of age was 1.11, with a 95% confidence interval of 0.97 to 1.27 (p = 0.14).

Children from homes with gas stoves had lower pulmonary function levels than did children not exposed to gas stoves at both examinations. The deficits at the first examination were 0.6% (p = 0.01) for FVC and 0.7% (p = 0.03) for FEV_1. At the second examination, the mean reduction was 0.3% (p = 0.17) for FVC and 0.3% (p = 0.26) for FEV_1. All comparisons were controlled for city-cohort and maternal smoking level. After adjustment for parental education, the estimated deficits associated with exposure to gas stoves were reduced by 30% for both FVC and FEV at the first examination and were no longer significant.

Discussion

These analyses show a consistent association between parental cigarette smoking and increased respiratory illness during childhood. Of the children in this sample, 43% had mothers who were current smokers (table 4), 59% had fathers who were current smokers, and 68% had at least one parent who was a current smoker. Thus, effects of sidestream cigarette smoke of the size observed in this study would represent a substantial public health burden.

Current maternal cigarette smoking was associated with a 20 to 35% increase in the risk of all respiratory illnesses and symptoms in the past year. A history of either parent smoking was associated with a similar increase in the reported prevalence of early childhood respiratory illness. Each of these respiratory health indexes is linearly related to the current amount of cigarette smoking by either both parents or the mother alone. In all of these analyses,

the association between impaired health and passive smoke exposure was stronger with maternal than with paternal or total parental smoking. Children of ex-smokers had respiratory illness and symptom frequencies that were typically between those of nonsmoking and currently smoking mothers. This was true for recent illness and symptom experience, as well as for early childhood illnesses. These findings are consistent, at least in part, with the hypothesis that exposure to cigarette smoke increases the risk for contemporaneous respiratory illness.

The stronger association with maternal rather than paternal smoking for these conditions is consistent with the independent findings of other investigators. Fergusson and coworkers (13) found respiratory illness in the first year of life to be highly associated with maternal smoking, and paternal smoking did not enter their model after controlling for maternal smoking. In their birth cohort of 1,265 children, the association between maternal cigarette smoking and respiratory illness was equivocal in the second year of life and no longer apparent during the third year. Weiss and associates (11) found persistent wheeze to be directly related to the number of smokers in the household among children 6 to 19 yr of age. Subsequent analyses of these data (36) confirmed that the association is strongly influenced by maternal smoking. Similar findings restricted to children 5 to 11 yr of age have been reported by Schenker and associates (37).

The somewhat stronger association of respiratory illness with maternal than with paternal smoking habits need not imply any special risk associated with maternal smoking. A more plausible interpretation is that the risk factor is exposure to sidestream cigarette smoke, and that children are more likely to be with their mothers than with their fathers at the times smoking occurs.

Although some investigators have not reported significant passive smoking relationships, their findings, given the size of the populations under investigation and methods used to adjust symptoms or disease rates, are consistent with our results. The total number of children younger than 10 yr of age available to Schilling and colleagues (19) was so small that a 20 to 35% increase in relative risk could not be detected. In contrast, Dodge (10) found a

significant passive smoking effect th was reduced (as in our study) by adju ing for parental history of respirato disease. The resulting coefficients, though relatively unchanged in magr tude and direction, were no longer si nificant. However, in a small group sixth graders, who completed their ow questionnaire, the gradient acro smoking categories persisted and w. significant.

Among the children participating the Six-Cities Study, there was a stror association between reported parent. respiratory illness (emphysema, bror chitis, or asthma) and higher preve lence of symptoms and illness (tables and 6). This may be explained in pa: by overreporting of the child's respira tory illnesses by smoking parents wh themselves have respiratory problem: or equivalently by the underreportin, of nonsmoking parents. Such reportin, bias cannot be separated in these an alyses from real differences in preva lence caused by familial aggregation or higher susceptibility within families. However, all the illnesses and symp toms still show increased prevalenc associated with parental smoking afte: adjusting for parental illness (table 6) This suggests that passive environmen tal exposure to smoking is a cause of respiratory illness.

Changes in level of FEV_1, although relatively small, were linearly related to amount smoked (figure 1). For maternal smoking of 1 pack per day, FEV_1 is estimated to be lower by 0.6 to 0.8%, or 10 to 20 ml for a child with FEV_1 between 1.5 and 2.5 L. Tager and coworkers (17) found a comparable association when they used maximal midexpiratory flow (MMEF), although initially they were unable to demonstrate the effect with FEV_1. Subsequent studies of these same children demonstrated the passive smoking effect for both FEV_1 and MMEF (36). Similar effects were found in a study of 4,000 children in a rural area of western Pennsylvania (37). However, the Tucson group (38) was unable to demonstrate this effect after adjusting for the pulmonary function level of the parent. Because cigarette smoking is associated with level of pulmonary function, the adjustment for parental level of function may have resulted in overadjustment.

Because the association between FEV_1 level and parental cigarette smoking had not been found in a previous analysis of a subset of these data (28),

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a series of comparative analyses were performed in that subset and in the entire data set providing the basis for this report. Those analyses established that the lack of association in the earlier investigation was attributable in approximately equal measure to the use of parental rather than to maternal smoking as the exposure variable and to the use of a normative model for pulmonary function level derived from a small subset of the study participants living in 2 cities.

The FEV_1 levels were not reduced in children of ex-smokers. However, in our study, we did not determine when these parents became ex-smokers and therefore cannot assess whether these ex-smokers were in fact ever smokers during the lifetime of their children. We have similar difficulty in trying to assess whether the effect noted is due to current exposure, cumulative exposure, or exposure at some earlier point in time. Because most parents' smoking habits are not likely to have changed significantly over the course of their children's first 11 yr of life, all 3 effects, or any combination thereof, could be operative.

We note, as have others (Vedal S and associates. Risk factors for childhood respiratory disease: analysis of pulmonary function. Am Rev Respir Dis, submitted for publication), that FVC was highest in children from households with parents who smoke. Some studies suggest that young adult smokers may have larger FEV_1 and FVC than do nonsmokers; however, the reason generally offered is that young adults with a history of respiratory illness are relatively disinclined to smoke. This would appear to be an unlikely explanation for the differences seen in young adults and would not explain a corresponding response to sidestream cigarette smoke.

In assessing the strength of the evidence given above for an effect of sidestream cigarette smoke on respiratory health, it is important to remember that the various indexes are not independent. The correlations, or phi coefficients (34), between pairs of illnesses and symptoms reported here varied between 0.14 and 0.37. Correlations were highest for illness before 2 yr of age and history of bronchitis, history of bronchitis and bronchitis in the last year, and wheeze and cough. Although these correlations are highly significant and indicate strong associations between the various outcomes, they are

not so large as to indicate that the different outcomes are redundant. The FVC and FEV_1 values are also highly correlated in young children. Because of the relationships among these outcomes, the many associations examined, and the large sample sizes, we have not emphasized individual p values in interpreting these data. Rather, we have looked for consistent patterns of association. The results for parental cigarette smoking fit that criterion.

These analyses provide less consistent evidence about the potential health significance of exposure to gas stoves. An estimated odds ratio for respiratory illness before 2 yr of age of 1.23 ($p < 0.01$) previously reported from this study (28, 29) has been reduced to 1.12 ($p = 0.07$) by the inclusion of additional children enrolled in the study but not available for the first analysis. A series of analyses comparing the 2 results established that this resulted primarily from the absence of an association between stove type and illness before 2 yr of age in the new cohorts rather than from small differences in models or statistical methods. No other respiratory illness or symptom was found to be significantly associated with stove type. Although respiratory illness before 2 yr of age may be a sensitive index of the effects of gas combustion products, such an association from these data should be interpreted cautiously because the analysis links exposure at 6 yr of age or older with illness before 2 yr of age.

These analyses confirm the earlier finding of approximately 0.6% lower FVC and FEV_1 levels at the first examination among children exposed to gas stoves. We also found a difference of 0.3% at the second examination. However, level of parental education is negatively associated with use of gas stoves and positively associated with pulmonary function level. Consequently, controlling for parental education reduces this association. This may represent confounding but may also represent overadjustment for a surrogate for gas stove use.

Controlling for city-cohort in these analyses substantially reduces, although it does not eliminate, the potential for bias caused by ethnic differences, examiner effects, equipment differences, and many other factors that influence indexes of respiratory health. However, the sensitivity of an analysis based on exposure categories, such as

parental cigarette smoking, is limited by the weak relationship between these categories and individual exposure to gases or particulate matter. The documented variation in particulate and nitrogen dioxide concentrations among homes with equal numbers of smokers or the same type of stove (4–9) implies that the exposure variables used in these analyses are subject to substantial measurement errors. Although the effects of these errors are not completely understood (39), they are likely to bias the estimated measures of association toward the null value. Thus, better understanding of the health significance of these indoor pollutants may require epidemiologic studies including refined measurement of personal exposure.

Finally, the medical significance of these findings related to passive smoking remains undetermined. The illness and symptom effects may be transient, and the effects on pulmonary function levels appear to be small. However, to the degree that these small effects persist or accumulate in early adult life, they may represent an important predictor of risk, particularly among those who take up cigarette smoking. Long-term follow-up and comparisons between children from homes where others smoke will be required to resolve this potentially important public health question.

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Fergusson, D.M., Horwood, L.J. "Parental Smoking and Respiratory Illness During Early Childhood: A Six-year Longitudinal Study" Pediatr Pulmonol 1: 99-106, 1985.

SUMMARY: The relationship between parental smoking habits and lower respiratory illness and symptoms during the first 6 years of life was studied in a birth cohort of New Zealand children.   This showed that maternal (but not paternal) smoking was associated with significant increase in rates of lower respiratory infection and lower respiratory symptoms during the child's first 2 years. This association persisted when a range of perinatal, social, and familial factors were taken into account statistically.   After two years there was no detectable association between parental smoking habits and lower respiratory infection.   Further, there was no evidence to suggest that children whose parents smoked had increased risks of asthma or rates of asthmatic attacks during early childhood.

Parental Smoking and Respiratory Illness During Early Childhood:
A Six-year Longitudinal Study

D. M. Fergusson, BA Hons, and L. J. Horwood, BA, BSc

Summary. The relationship between parental smoking habits and lower respiratory illness and symptoms during the first 6 years of life was studied in a birth cohort of New Zealand children. This showed that maternal (but not paternal) smoking was associated with significant increase in rates of lower respiratory infection and lower respiratory symptoms during the child's first 2 years. This association persisted when a range of perinatal, social, and familial factors were taken into account statistically. After two years there was no detectable association between parental smoking habits and lower respiratory infection. Further, there was no evidence to suggest that children whose parents smoked had increased risks of asthma or rates of asthmatic attacks during early childhood. (Key words: asthma, children, cigarette smoking, lower respiratory illness, parental smoking) *Pediatr Pulmonol 1985; 1:99–106*

A number of studies have examined the relationship between parental smoking and lower respiratory illness in children[1-13] and, in general, the results have suggested that parental smoking may be harmful to children. Perhaps the best-documented findings relate to the increased rates of lower respiratory infection and symptoms that have been observed in children under 2 years of age whose parents (and, particularly, the mothers) smoke.[1-4,10,11] This association has been found in a variety of studies that have used both retrospective and concurrent measures of medical consultation for lower respiratory infection,[1-4,10,11] maternal reports of lower respiratory symptoms,[4,9] and hospital attendance data.[3] The correlation has been shown to persist when a large number of potentially confounding factors have been controlled, including family social background,[2-4,10,12] family composition,[2-4] lower respiratory illness in the child's family,[2,3,10] infant feeding practices,[2,9] and perinatal history.[2,3] In at least two studies the association in children between early lower respiratory illness and parental smoking has been shown to disappear at around 2 years of age.[2,9]

A further series of studies have suggested that, in school-aged children, parental smoking and, particularly, maternal smoking is associated with increased rates of lower respiratory symptoms,[7-13] lower respiratory infection,[10-15] and reduced pulmonary function.[11,14-18] The introduction of control factors, including measures of family social background[7,9,16] and the children's smoking habits,[7,11,12,13,18] has not appreciably altered these correlations. At the same time, not all studies of school-aged populations have found linkages between parental smoking and pulmonary function.[17,18]

A number of investigators have also examined the relationship between parental smoking and the onset and frequency of asthma during childhood, and the majority of studies[10,19-21] have failed to find any tendency for the children of parents who smoke to be more prone to asthma than those of nonsmokers. An exception to this trend, however, was reported by Gortmaker et al.[22] who found a small but statistically significant tendency for children whose parents smoked to suffer greater rates of asthma.

Although the general conclusion that may be drawn from this literature is that smoking is harmful for children, some aspects of the findings suggest that this relationship may not be a simple one. In particular, the emerging evidence tends to suggest that the effects of parental smoking vary with the age of the child (being most marked during early childhood), the source of the parental smoke (with maternal smoking having a greater influence than paternal smoking), and the disease that is studied (with lower respiratory infection and symptoms being more influenced by parental smoking habits than childhood asthma).

To place these issues in perspective, this pa-

per reports the results of a six-year longitudinal study of the relationship between parental smoking habits and lower respiratory illness in children in a sample of New Zealand children. The aims of the paper are: 1) To examine the relationship between rates of lower respiratory infection or symptoms in children, parental smoking habits, and the children's ages and to devise a statistical model describing the linkages between these variables. 2) To examine the association between parental smoking and the onset of asthma and the frequency of asthmatic attacks during early childhood.

Method

The data were collected during the first eight stages of the Christchurch Child Development Study. A birth cohort of children born in the Christchurch (New Zealand) urban region in mid-1977 was studied at birth, 4 months, and annual intervals to the age of 6 years using a combination of a home-based interview with the mother supplemented by information from hospital records, general practitioner notes, and other documentary sources. The general methods of data collection and the quality control of the data have been described in previous papers.[11,12] The following information was used in the present analysis.

Medical Consultation for Lower Respiratory Infection. Information on medical consultations for bronchitis, bronchiolitis, and pneumonia was collected for each child for each year of life. This information was gathered from several sources including maternal recall, diaries of the children's health that were kept each year by the mothers, and information from general practitioner records.

Maternal Reports of Lower Respiratory Symptoms. Mothers were questioned about whether their child had had a "chesty cold" or "wheezy chest" at each year of life irrespective of whether a medical consultation had been involved. Separate items for chesty cold and wheeze were used for children up to 2 years of age. However, during the first year of the study, our interviewers reported that many mothers had difficulty distinguishing between wheeze and general chestiness. To overcome this possible ambiguity, from the second year onward we used a single item that covered both chesty cold and wheeze. The measure used in this analysis is based on whether at each year of life, the mother reported that her child had suffered from chesty colds or wheeze irrespective of whether medical attention was sought for these conditions.

Asthma During Early Childhood. To measure whether a child was prone to asthma and, if so, the frequency of the asthmatic attacks, four measures were developed.

1.—whether the child had ever attended a medical practitioner for the treatment of wheeze that had been diagnosed as asthma or wheezy bronchitis. (Wheezy bronchitis was included in the definition of asthma on the basis of Williams and McNicol's[13] conclusion that the two conditions are indistinguishable: however, only 8% of all diagnoses were for wheezy bronchitis.)

2.—whether the mother had ever reported that her child had suffered an asthmatic attack irrespective of whether this attack had been treated medically.

3.—the frequency of medical attendance from birth to 6 years for episodes of wheeze that were diagnosed as asthma or wheezy bronchitis.

4.—the frequency of maternal reports of asthmatic episodes during the period from birth to 6 years irrespective of whether medical attendance was sought.

The first two measures defined the proportion of children who, according to medical diagnosis or maternal belief, were prone to asthma: the second two measures described the frequency of asthmatic attack among those children who were susceptible to asthma.

Parental Smoking. At each year, mothers were questioned about their daily cigarette intake and the intake of the child's father.

Control Factors

To take account of the possibility that any apparent correlations between parental smoking and lower respiratory illness could have arisen from the effects of common confounding variables, the following measures were used for the purpose of statistical control.

Perinatal Status. Measures of the children's birthweights and estimated gestational ages were obtained from hospital records.

Family Composition and Social Background. As part of the routine data collected during the course of the study, information was available on maternal ages, family sizes, maternal educational levels, the children's ethnicity, and family socioeconomic statuses as measured by the Elley and Irving[14] scale of socioeconomic status for New Zealand.

Family Atopy. At the initial interviews with

table 1—Risks per 100 Children of Medical Consultations for Bronchitis/Pneumonia and Maternal Reports of Lower Respiratory Symptoms by Age of Child and Parental Smoking Habits (Number of Children in Sample in Parentheses):

	Medical Consultation for Bronchitis/Pneumonia				Maternal Reports of Lower Respiratory Symptoms			
	Maternal Smoking (cigs/day)				Maternal Smoking (cigs/day)			
	0	1-10	11+	Total	0	1-10	11+	Total
Children 0-2 years								
Paternal smoking (cigs/day)								
0	14 6	22 7	25 2	17 0	60 9	66 7	70 4	62 9
	(575)	(75)	(115)	(765)	(575)	(75)	(115)	(765)
1-10	9 1	14 0	23 5	12 7	54 6	74 4	70 6	63 5
	(66)	(43)	(17)	(126)	(66)	(43)	(17)	(126)
11+	18 3	25 0	28 4	22 9	67 5	63 5	71 6	70 0
	(120)	(52)	(81)	(253)	(120)	(52)	(81)	(253)
Total	14 7	21 2	26 3	17 8	61 4	67 7	70 9	64 1
	(761)	(170)	(213)	(1144)	(761)	(170)	(213)	(1144)
Children 2-4 years								
Paternal smoking (cigs/day)								
0	13 7	9 9	17 0	13 8	53 2	59 2	58 9	54 6
	(590)	(71)	(112)	(773)	(590)	(71)	(112)	(773)
1-10	16 0	8 7	20 8	15 6	60 0	34 8	58 3	54 9
	(75)	(23)	(24)	(122)	(75)	(23)	(24)	(122)
11+	15 2	13 9	15 6	15 1	59 4	52 8	62 5	55 6
	(105)	(36)	(64)	(205)	(105)	(36)	(64)	(205)
Total	14 2	10 8	17 0	14 3	53 8	53 1	60 0	54 8
	(770)	(130)	(200)	(1100)	(770)	(130)	(200)	(1100)
Children 4-6 years								
Paternal smoking (cigs/day)								
0	11 1	17 0	10 7	11 5	51 5	55 9	53 7	52 2
	(586)	(59)	(121)	(766)	(586)	(59)	(121)	(766)
1-10	6 1	17 4	13 0	9 8	51 5	60 9	70 0	57 1
	(66)	(23)	(23)	(112)	(66)	(23)	(23)	(112)
11+	12 3	12 5	7 8	10 8	52 8	52 5	54 6	53 4
	(106)	(40)	(77)	(223)	(106)	(40)	(77)	(223)
Total	10 8	15 6	10 0	11 2	51 7	55 7	55 7	53 0
	(758)	(122)	(221)	(1101)	(758)	(122)	(221)	(1101)

the children's mothers. Information was collected on the presence (both past and present) of asthma. allergic rhinitis. and eczema in the mother. biological father. and siblings.

Breastfeeding History. From information collected from hospital notes and maternal interviews. estimates of the duration of time (if at all) the child was breastfed were obtained.

Pets in the Home. At each year. mothers were questioned about the presence of pet cats or dogs in the children's families. and an estimate of the extent of exposure to these animals was created for each child by summing the number of years the pets had been in the child's family.

Family Life Events. From two years onward. mothers were questioned about the occurrence of adverse or stressful life events using a 26-item check list based on an abbreviated version of the Holmes and Rahe[12] social readjustment rating scale. For each year. an estimate of the extent of exposure to stressful life events was created by summing the number of such events reported.

Sample Sizes

The initial cohort comprised 1,265 children. but as a result of emigration from New Zealand and losses to follow up. this cohort was reduced in 6 years to 1,115 children. This reduced sample represented 88% of the original cohort and 95% of those cohort members still alive and resident in New Zealand. However. throughout the analysis. sample sizes varied with the age of the children because complete data on parental smoking and respiratory illness for the full six-year period were not available for every child. (These were children who had left New Zealand. and who re-entered the study on their return.) The variations in sample size are reflected in tables 1. 4. and 5.

Results

Medical Consultation for Lower Respiratory Infection and Maternal Reports of Lower Respiratory Symptoms. Table 1 shows the associations between parental smoking habits and rates

table 2—Risks per 100 Children Aged 0-2 years of Bronchitis/Pneumonia and Lower Respiratory Symptoms by Maternal Smoking Adjusted for Family Size, Perinatal Status, Breastfeeding, and Family Social Circumstances

Maternal Daily Cigarette Intake	Bronchitis/Pneumonia	Lower Respiratory Symptoms
Nonsmoker	15 3	61 6
1-10 per day	19 5	65 0
11+ per day	24 5	68 2

of medical consultation for bronchitis and pneumonia and maternal reports of lower respiratory symptoms in their child during the period from birth to 6 years. (The data are presented in two-year blocks for simplicity, but a parallel analysis of the year-by-year trends in the data produced similar results.) Inspection of the table suggests that parental smoking and particularly maternal smoking was associated with increased rates of medical consultation and increased maternal reports of lower respiratory symptoms in the children we studied during the first two years of life. However, after the children reached 2 years of age, there appeared to be little or not association between parental smoking habits and the rates of lower respiratory illness or symptoms. These conclusions were confirmed by fitting a series of hierarchical log linear models[24] to the data on rates of lower respiratory illness shown in the table. This procedure led to the following conclusions: 1) During the children's first 2 years of life, maternal smoking was associated with significant increases in rates of medical consultation for lower respiratory infection (log likelihood ratio χ^2 = 15.90, df = 2, $P < 0.001$) and maternal reports of lower respiratory symptoms (log likelihood ratio χ^2 = 8.27, df = 2, $P < 0.05$). Paternal smoking did not make a contribution to the variability in rates of illness when considered alone or in combination with maternal smoking. 2) After the children reached 2 years of age, there were no significant associations between parental smoking habits and rates of lower respiratory illness or symptoms.

The results in table 1 do not take into account the possible effects of other social or familiar factors that may be correlated with maternal smoking habits and childhood lower respiratory illness or symptoms. To examine this issue, the data for the first 2 years were reanalyzed using logistic regression methods[17] in which maternal smoking together with the measures of family social background, family composition, infant feeding practices, and perinatal history were related to rates of medical consultation for bronchitis and pneumonia and rates of maternal

reports of symptoms. Results of this analysis clearly showed that even when all control factors were taken into account, there was a significant association during the children's first two years between maternal smoking habits and rates of lower respiratory infection ($P < 0.01$) and a marginally significant ($P < 0.06$) association between maternal smoking habits and rates of lower respiratory symptoms. From the fitted model, estimates were obtained using the methods described by Lee[26] of the association between maternal smoking and rates of lower respiratory infection and symptoms that were adjusted for the effects of the control factors. The adjusted rates are shown in table 2 and indicate that the introduction of the control factors had a negligible effect on the general dose/response relationship between maternal smoking habits and rates of lower respiratory infection and symptoms in children under the age of 2 years.

Our initial analyses examined the data in a series of cross-sectional two-year blocks. To analyze the dynamic relationships that existed between maternal smoking and rates of lower respiratory illness and symptoms throughout the child's first 6 years, the data was used to form a 3 × 2 contingency table,[*] which described the associations between maternal smoking during the child's first 2 years and rates of lower respiratory infections and symptoms throughout the child's first 6 years. This table was fitted using log linear modeling methods. A summary of the analysis is shown in table 3, which gives values

table 3—Fitted Log Linear Model of Maternal Smoking, Medical Consultations for Lower Respiratory Illness, and Maternal Reports of Lower Respiratory Symptoms (0-6 Yrs)

Factor		χ^2	df	P
First-order effects				
Maternal smoking	(A)			
Medical consultations 0-2 yrs	(B)			
Symptoms (0-2 yrs)	(C)			
Medical consultations (2-4 yrs)	(D)	682 68	183	$P < 0.0001$
Symptoms (2-4 yrs)	(E)			
Medical consultations (4-6 yrs)	(F)			
Symptoms (4-6 yrs)	(G)			
Second-order effects				
AB		15 42	2	$P < 0.01$
AC		7 96	2	$P < 0.05$
BC		176 75	1	$P < 0.0001$
BD		17 82	1	$P < 0.001$
CE		9 01	1	$P < 0.01$
DE		132 40	1	$P < 0.0001$
DF		29 28	1	$P < 0.001$
EG		29 24	1	$P < 0.001$
FG		132 97	1	$P < 0.0001$
Residual		131 73	170	$P > 0.99$
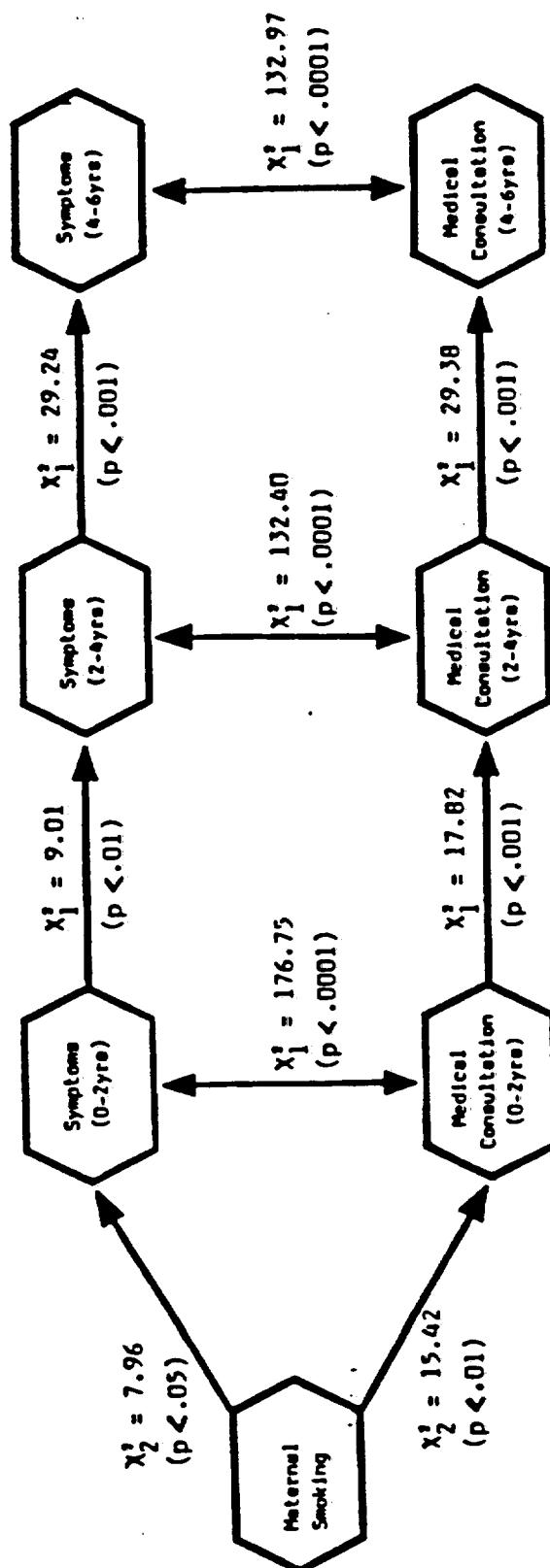
of the log likelihood ratio chi-square statistics for the various effects in the fitted model. The results can be readily interpreted from figure 1, which shows the fitted model using the conventions described by Freeman and Jekel." In this diagram, variables that were significantly related are shown linked by solid lines, and the size of the association is indicated by the log likelihood ratio chi square value and its corresponding level of significance. Variables that were not significantly related are not linked by lines. The following conclusions can be drawn from the figure. 1) Maternal smoking was associated with significant increases in rates of lower respiratory illness ($P < 0.01$) and symptoms ($P < 0.05$) during the children's first 2 years. 2) Within each measuring period there were very strong associations ($P < 0.0001$) between medical consultations for lower respiratory illness and maternal reports of lower respiratory symptoms. These associations arose because if the child had attended a medical practitioner for lower respiratory illness, his or her mother almost invariably reported lower respiratory symptoms. 3) There were significant associations ($P < 0.001$) between rates of medical consultation for lower respiratory illness across measurement periods. Thus, lower respiratory infection during the first 2 years was significantly associated with lower respiratory infection during the period from 2 to 4 years, which in turn was associated with lower respiratory infection during the period from 4 to 6 years. A similar causal-chain model links the measures of maternal reports of lower respiratory symptoms.

As may be seen from Table 3, the model depicted in figure 1 produced a very satisfactory fit to the observed data ($\chi^2 = 131.73$; $df = 172$, $P = 0.99$).

Asthma During Early Childhood. Table 4 compares the number of children having at least one asthmatic episode (defined both on the basis of medical consultation and maternal report) by the age of 6 years with parental smoking habits. Inspection of the table shows no clear tendency for the proportions of asthmatic children to vary with parental smoking habits, and this was confirmed by log linear modeling of the results, which indicated that there was no significant association between being asthmatic and parental smoking habits.

figure 1—Fitted log linear model of maternal smoking, medical consultation for lower respiratory illness, and maternal reports of lower respiratory symptoms in children 0-6 years of age.

table 4—Risks Per 100 Children of Having at Least One Asthmatic Episode by the Age of 6 Years by Parental Smoking Habits (Number of Children in Sample in Parentheses)

Paternal smoking (cigs/day)	Medical Consultation				Maternal Report			
	Maternal Smoking (cigs/day)				Maternal Smoking (cigs/day)			
	0	1-10	11+	Total	0	1-10	11+	Total
0	12.6 (460)	9.0 (67)	6.8 (74)	11.4 (601)	13.5 (460)	10.5 (67)	8.1 (74)	12.5 (601)
1-10	15.1 (86)	17.2 (64)	16.9 (65)	16.3 (215)	15.1 (86)	17.2 (64)	16.9 (65)	16.3 (215)
11+	17.2 (93)	12.3 (57)	9.1 (66)	13.4 (216)	17.2 (93)	14.0 (57)	10.6 (66)	14.4 (216)
Total	13.6 (639)	12.8 (188)	10.7 (205)	13.0 (1,032)	14.2 (639)	13.8 (188)	11.7 (205)	13.7 (1,032)

However, the results in table 4 do not take into account the possibility that, while parental smoking may not influence the child's predisposition to asthma, it may influence the frequency of asthmatic attacks among those susceptible to asthma. This issue is examined in table 5, which shows the frequency of asthmatic attacks per 100 children (measured both on the basis of maternal report and frequency of medical consultation) related to parental smoking habits. While there was substantial variability in the rates of asthmatic attacks depending on the combinations of parental smoking, there was no clear trend in the results that would suggest increased parental smoking was associated with increases in the rate of asthmatic attacks. This impression was confirmed by log linear modeling of the data in table 5, which showed there were no significant associations between parental smoking and the frequency of asthmatic attacks.

To examine the possible effects of various confounding factors on the associations between parental smoking and the occurrence of asthma in children and the rates of asthmatic attacks, the data were further analyzed using regression methods in which a number of control factors, including gender, family history of asthma, early eczema, early respiratory infection, breastfeeding history, pets in the family, family life events, and family social background were introduced as factors in stepwise analyses. The analysis of the risk data in table 4 was conducted using multiple logistic regression, whereas the frequency of attack data (table 5) were analyzed using multiple linear regression methods based on the square root of the number of episodes of asthma occurring during the period from 0–6 years. All analyses indicated that there were no significant relationships between parental smoking habits and risks of childhood asthma or rates of asthmatic attacks even when the set of control factors was taken into account statistically.

Discussion

The findings of this six-year longitudinal study indicate that the effects of parental smoking on childhood respiratory illness depended on the child's age, the source of parental smoke, and the outcome studied. There was clear evidence of a relationship during the child's first 2 years between maternal (but not paternal) smoking and both an increased rate of medical consultations for bronchitis/pneumonia and increased reports of lower respiratory symptoms. However, after this time, maternal smoking did not make a significant contribution to the rates of medical consultation or reports of lower respiratory symptoms. Paternal smoking was not related to lower respiratory illness at any time, and neither paternal nor maternal smoking was related to the risk of asthma or the frequency of asthmatic attacks during the child's first 6 years.

The finding of an association between lower respiratory illness or symptoms and parental smoking during the first two years of life confirms the findings of a number of previous studies,[1-3][10][12] and, as remarked earlier, the correlation appears to be resilient to the effects of statistical and other controls. Collectively, the available evidence strongly suggests that maternal smoking increases rates of lower respiratory illness and symptoms in children up to the age of 2 years. However, the mechanisms involved are as yet unclear. Colley et al.[7] proposed a genetic explanation in which parental smoking is related to a genetic disposition to lower respiratory illness, which is reflected in higher rates of morbidity among the offspring of smokers. However, this explanation seems highly unlikely given that, according to most studies, maternal smoking is more important in this regard than is paternal smoking, which would suggest a mode of inheritance in which a predisposition to lower respiratory illness is sex linked to the child's mother. Fergusson et al.[2] have suggested

table 5—Rate Per 100 Children Aged 0–6 Years of Asthmatic Attacks by Parental Smoking (Number of Children in Sample in Parentheses)

	Medical Consultation				Maternal Report			
		maternal smoking (cigs/day)				maternal smoking (cigs/day)		
	0	1-10	11+	Total	0	1-10	11+	Total
Paternal smoking (cigs/day)								
0	57.4 (460)	49.3 (67)	56.8 (74)	56.4 (601)	124.6 (460)	79.1 (67)	101.4 (74)	116.6 (601)
1-10	76.7 (86)	34.4 (64)	79.3 (65)	62.8 (215)	166.3 (86)	98.4 (64)	201.5 (65)	156.7 (215)
11+	95.7 (93)	38.6 (57)	56.1 (66)	68.5 (216)	163.4 (93)	59.7 (57)	130.2 (66)	125.9 (216)
Total	65.6 (639)	41.0 (188)	61.5 (205)	60.3 (1,032)	135.8 (639)	79.8 (188)	142.4 (205)	126.9 (1,032)

a hypothesis in which prolonged exposure to cigarette smoke has an irritant effect that exacerbates the respiratory infections that normally occur during early childhood, making it more likely that lower respiratory symptoms will develop.

However, whereas previous studies[5-10] have reported associations between lower respiratory symptoms, lower respiratory illness or impaired pulmonary function, and parental smoking for school-aged children, we were unable to find any association between parental smoking and respiratory illness or symptoms during the period from 2–6 years. It seems possible that this may reflect the age of the children studied. In particular, it seems likely that prolonged exposure to parental smoke may have an accumulative effect[14] on pulmonary function and susceptibility to lower respiratory illness, and it is possible that our sample of children was too young for any increase in rates of morbidity or symptoms to be detected. In contrast, the previous studies that have demonstrated associations in school-aged children have examined older populations or populations with a wider age range than our sample.

It has been suggested that the association between parental smoking and lower respiratory symptoms and illness in school-aged children may reflect the indirect consequences of early exposure to cigarette smoke. Tager et al.[14] argue that such early exposure coupled with increased risks of early lower respiratory illness may cause structural changes that are reflected in increased rates of lower respiratory symptoms and reduced pulmonary function during later childhood. The results of the longitudinal log linear analysis presented in this paper cast some light on the plausibility of this hypothesis. In particular, the model suggested that maternal smoking was associated with an increased risk of lower respiratory illness and symptoms during the child's first 2 years, and that early respiratory illness or symptoms during the first 2 years are associated with subsequent illness or symptoms. At first sight these results would appear to support the hypothesis that early exposure to parental smoke leads to later respiratory illness. However, this view does not take into account the statistical "slippage" that occurs within this system of relationships. Thus, while maternal smoking does influence early respiratory illness, and early respiratory illness is related to later respiratory illness, maternal smoking made a negligible direct or indirect contribution to later respiratory illness for our cohort. This suggests that the tendency for rates of lower respiratory illness or symptoms to be correlated over time cannot be attributed to the common effects of maternal smoking on respiratory function.

A more plausible explanation of the existing data would appear to be that there are two mechanisms involved in the correlations between parental smoking and lower respiratory illness and symptoms in children. First, during early childhood there is a short-term effect by which exposure to cigarette smoke has the effect of increasing the likelihood of early respiratory illness. This effect is relatively short lived and disappears at around the age of 2 years. However, in the light of the findings of Tager et al.[14] there is also evidence to suggest that prolonged exposure to parental smoking may have the effect of gradually compromising the lower respiratory system of children so that around the middle-school years, children become at greater risk of lower respiratory illness and reduced pulmonary function.

In confirmation of three previous studies,[10,19,21] we were unable to show any correlation between parental smoking and either the onset or frequency of asthmatic attacks during early childhood. These results suggest that, while parental smoking may predispose children to develop lower respiratory illness and symptoms, it is not implicated in the development of asthma or the

frequency of asthmatic attacks in young children. At the same time. Gortmaker et al.[22] were able to show a small but nonetheless significant association between parental smoking habits and asthma in a cross-sectional sample of children aged from 0–17 years. It seems possible that these differences may reflect age differences between samples. If, as was conjectured previously. prolonged exposure to cigarette smoke has a subtle. long-term effect on respiratory function. It is possible that an association between parental smoking and childhood asthma exists only in older children who have experienced sufficient exposure to parental smoke to increase their susceptibility to asthmatic attacks. It should also be noted that the apparent correlation between parental smoking and asthma reported by Gortmaker et al.[22] could be a disguised correlation between asthma and smoking in the child,[30,31] as this factor was not controlled for in their analyses.

Finally. while the results of this study support the general conclusion that parental smoking may be harmful to children. the results suggest the possibility of complex relationships between the child's age. duration of exposure to smoke. and various measures of respiratory illness and function. Such relationships can only be clarified by further longitudinal studies that examine the way in which varying exposure times to parental smoking have dynamic effects on both the susceptibility to lower respiratory illness and pulmonary function throughout childhood.

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ABSTRACT: A prospective study of 1,144 infants and their families was performed. Smoking and family histories were evaluated with respect to the incidence of lower respiratory disease during the first year of life. It was found that (1) tracheitis and bronchitis occurred significantly more frequently in infants exposed to cigarette smoke in the home, (2) maternal smoking imposed greater risks upon the infant than paternal smoking, (3) occurrence of neither tracheitis nor bronchitis showed a consistent relationship to the number of cigarettes smoked, (4) a family history that was positive for respiratory illness (chronic cough or bronchitis) significantly influenced the incidence of bronchitis, (5) too few cases of laryngitis and pneumonia were seen to warrant any opinions regarding the adverse influence of either smoking or a family history that was positive for respiratory illness, and (6) occurrence of bronchiolitis was not affected by the presence of a smoker nor influenced by a family history that was positive for respiratory illness. It is concluded that passive smoking is dangerous to the health of infants and that infants born to families with a history that is positive for respiratory illness (chronic cough or bronchitis) are at risk of developing bronchitis.

Involuntary Smoking and Incidence of Respiratory Illness During the First Year of Life

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ABSTRACT. A prospective study of 1,144 infants and their families was performed. Smoking and family histories were evaluated with respect to the incidence of lower respiratory disease during the first year of life. It was found that (1) tracheitis and bronchitis occurred significantly more frequently in infants exposed to cigarette smoke in the home, (2) maternal smoking imposed greater risks upon the infant than paternal smoking, (3) occurrence of neither tracheitis nor bronchitis showed a consistent relationship to the number of cigarettes smoked, (4) a family history that was positive for respiratory illness (chronic cough or bronchitis) significantly influenced the incidence of bronchitis, (5) too few cases of laryngitis and pneumonia were seen to warrant any opinions regarding the adverse influence of either smoking or a family history that was positive for respiratory illness, and (6) occurrence of bronchiolitis was not affected by the presence of a smoker nor influenced by a family history that was positive for respiratory illness. It is concluded that passive smoking is dangerous to the health of infants and that infants born to families with a history that is positive for respiratory illness (chronic cough or bronchitis) are at risk of developing bronchitis. Pediatrics 1985;75:594–597; respiratory disease, smoking, infants, tracheitis, bronchitis.

On Jan 11, 1964, the Surgeon General's Advisory Committee on Smoking and Health concluded: "Cigarette smoking is a health hazard of sufficient importance in the United States to warrant appropriate remedial action."[1] Since that time, abundant evidence has been collected demonstrating the adverse effect on the health of nonsmokers exposed to cigarette smoke.[2-4] More recently, there has been considerable interest in the health of children in families with chronic smokers.[5-9] The deleterious effects of maternal smoking on the fetus and newborn baby have been demonstrated.[10] Moreover, several studies[11,12] have shown that exposure to cigarette smoke during the first year of life significantly increases an infant's risk of developing pneumonia or bronchitis.[9,12] Additionally, some studies[3] have suggested that passively inhaled cigarette smoke can lead to the development of recurrent respiratory syndromes such as chronic infections, bronchopulmonary disease, and cough.

The adverse influence of family factors on the incidence of lower respiratory illness during the first year of life has been well documented.[13] Evidence suggests that genetic factors often are significant in the development of asthma and/or bronchitis with wheezing (wheezy bronchitis). The effect of parental smoking superimposed on this type of genetic predisposition needs further clarification.

This study was designed to evaluate prospectively the effects of parental smoking and parental and sibling respiratory symptoms, including chronic cough, asthma, and bronchitis, on the incidence of lower respiratory illness during the first year of life.

METHOD

This study was conducted from 1976 through 1981 among patients in the pediatric practice of the first four authors. All newborns seen by our group pediatric practice for their first well baby examination (age 2 weeks to 1 month) were enrolled in this study. The office is located in a suburb approximately 30 miles from Washington, DC. Nearly all of the households represented live in a fairly homogeneous suburb with the following demographic

characteristics: (1) population by race: white, 89%; black, 5%; Oriental, 5%; other, 1%; (2) population by age: children aged 17 years or less, 27%; adults aged 18 to 64 years, 68%; adults aged 65 years or more, 5%; (3) total population of 56,424 (all within urbanized areas); (4) population by sex: females, 53%; males, 47%; (5) population aged 1 year or less, 2%; (6) median income of $34,700 per household. In our group private practice, there are 7,000 families enrolled with 11,500 children represented. The demographic characteristics of our practice population match those of the suburb described. Seventy families (1% of patient population) receiving Medicaid are enrolled in our practice.

On admission to the study, each patient had a stamp affixed to his chart to record a detailed family respiratory history (chronic cough, chronic bronchitis, asthma, other lower respiratory tract symptoms) and smoking history (father, mother, and others in household). All occurrences of lower respiratory tract infection (laryngitis, epiglottitis, laryngotracheobronchitis [croup], tracheitis, bronchitis, bronchiolitis, and pneumonia) for which there was an office visit during the infant's first year of life were recorded. No attempt was made to study the possible effect of other neonatal problems (hyaline membrane disease, meconium aspiration, infections) on the development of lower respiratory tract disease.

For the purposes of our study, lower respiratory tract infections were defined clinically (according to Moffet[13]) as follows: (1) laryngitis was recognized by hoarseness and laryngotracheobronchitis (croup) was characterized by brassy cough and inspiratory crowing; (2) epiglottitis was defined by the visualization of a red and edematous epiglottis associated with the pooling of oropharyngeal secretions and hoarseness; (3) tracheitis was characterized by brassy cough (without hoarseness) and coarse breath sounds (but without rales, rhonchi or wheezing); (4) bronchitis was defined by the association of cough with coarse rhonchi that clear with coughing (with or without wheezing) but without audible rales (for the purposes of this study rhonchi are defined as coarse, moist popping

sounds, usually occurring on inspiration; rales are fine popping sounds characteristically occurring at the end of inspiration); (5) bronchiolitis was characterized by tachypnea, poor air exchange, low diaphragm, clinical evidence of expiratory difficulty, and coarse inspiratory or expiratory breath sounds throughout the chest (this condition only was recognized in children 2 years of age or less); and (6) pneumonia was diagnosed on the basis of fine end-inspiratory rales (frequently associated with fever and cough) with or without roentgenographic confirmation.

Children lost to follow-up during their first year were excluded from the study. The data were analyzed with the assistance of the Research Division of the Children's Hospital National Medical Center in Washington, DC. The occurrence of each respiratory disease in the study population was tabulated and expressed as incidence (number of occurrences in first year of life per 1,000 infants).

RESULTS

A total of 1,420 infants and their families qualified for the study. During the course of the investigation, 276 patients (24%) were lost to follow-up; 1,144 patients completed the entire year of surveillance and represent the study population. Of those, 731 (64%) were from "nonsmoking" families; 413 (36%) were from families with at least one smoker. Both father and mother smoked in 127 households (11%). The study population breakdown by smoking habit is shown in Table 1. No more than one infant per family was enrolled in the study. Correlation coefficients were calculated to estimate the strength of the relationship between family smoking and respiratory disease.

Tracheitis was 89% more frequent among infants exposed to household smokers (Pearson's correlation coefficient for tracheitis v smoking, $r = .06$, $P = .02$); bronchitis was 44% more frequent in households with smokers than in nonsmoking households. (Pearson's correlation coefficient for bronchitis v smoking: $r = .06$, $P = .02$).

Illnesses other than tracheitis and bronchitis

TABLE 1. Breakdown of Study Population Households by Smoking Habit*

Smoker	No Smoking	Cigarette Smoking				Cigar Smoking	Pipe Smoking	Totals
		Yes†	1-10/d	11-20/d	>20/d			
Mother	927 (81%)	96 (8%)	12 (1%)	97 (9%)	12 (1%)	...	...	217 (19%)
Father	821 (72%)	110 (10%)	13 (1%)	116 (10%)	45 (4%)	13 (1%)	26 (2%)	323 (28%)
Totals‡	731 (64%)	...	...			...		413 (36%)

* Values are number of households; values in parentheses indicate percent of total households.
† Yes indicates smoker, but unknown amount.
‡ Totals represent total number of households and percent of households.

TABLE 2. Incidence of Respiratory Disease by Family Smoking History*

Type of Family	Bronchitis (n = 95)	Tracheitis (n = 32)	Laryngitis (n = 6)	Croup (n = 40)	Pneumonia (n = 7)	Bronchiolitis (n = 42)
Nonsmokers	71.3	21.0	4.2	35.0	7.0	37.8
Smokers	102.6	39.6	7.0	35.0	4.7	35.0
Totals	83.0	28.0	5.2	35.0	6.1	36.7

* Incidence is reported as occurrences per 1,000 infants.

either were rare (laryngitis and pneumonia) or were not affected by the presence of a smoker (bronchiolitis). Epiglottitis was not diagnosed in the study population. None of the children studied had recurrent bouts of lower respiratory tract disease. The incidence of respiratory disease by amoking history is shown in Table 2.

Bronchitis occurred 44% more frequently in households in which the mother smoked (111) than in households in which the mother did not (77; x^2 = 19.0, df = 8, P = .014), but occurred only 10% more frequently in households in which the father was the smoker (88 v 80; x^2 = 15.4, df = 12, P = NS). Similarly, tracheitis occurred 92% more frequently (46 v 24; x^2 = 16.5, df = 8, P = .036) in households in which the mother smoked as opposed to a 7% increase (30 v 28; x^2 = 11.8, df = 12, P = NS) in households in which the father smoked.

Approximately 40% of the parents who smoked failed to disclose the amount they smoked. Consequently, analysis of the effect of "smoke dose" on respiratory illness was restricted to the 121 families in whom amount of maternal smoking was documented. Of the 217 mothers in the study population who smoked, 12 (5.5%) reported smoking more than one pack per day; 96 mothers (44.2%) admitted to smoking without specifying the amount. Occurrence of neither tracheitis nor bronchitis showed a consistent relationship to the number of cigarettes smoked. Analyses based on smoking of the mother or father all showed nonmonotonic relationships between number of cigarettes smoked and incidence of respiratory disease. For example, incidence of bronchitis among families in which the mother reported smoking more than one pack per day was actually somewhat lower than the incidence for mothers who smoked less than one pack per day. We noted no relationship between exposure to cigarette smoke and age of disease onset.

The relationship of family history of respiratory illness (chronic cough and bronchitis) also was found to influence the incidence of bronchitis in the children studied. A family history that was positive for respiratory disease was associated with twice the incidence of infant respiratory illness. Although a positive trend was noted with regard to occurrence of tracheitis and family history of respiratory disease, the differences were not statisti-

TABLE 3. Incidence of Respiratory Illness as Function of Family History*

	Tracheitis		Bronchitis	
	No (1,112)	Yes (32)	No (1,049)	Yes (95)
Family history of:				
Chronic cough (n = 30)	20	30	90†	160
Chronic bronchitis (n = 106)	30	40	80†	160
Asthma (n = 236)	30	40	90	90
Other respiratory illness (n = 15)	30	0	90	180

* Incidence rounded to nearest 5 and expressed as occurrences per 1,000 infants. Absolute number of occurrences is shown in parentheses.
† Significance by x^2, P = .01.

cally significant. A family history of asthma had no documented effect on the incidence of bronchitis or tracheitis in the study population. The incidence of respiratory illness as a function of family history is shown in Table 3. The numbers of children who had both family history of respiratory disease and parents who smoked were too low for statistical analysis of their interaction on occurrence of respiratory disease.

DISCUSSION

Morbidity and mortality statistics reveal an increasing incidence of pneumonia and bronchitis in infants less than 1 year of age. Although mortality from these conditions has decreased significantly in the past 30 years in most age groups, infants continue to suffer and die in disproportion to the rest of the pediatric population.[9] Several studies[6,8,11] have documented the relationship between parental smoking and respiratory illness in infants. Leeder et al,[12] studying a population of 2,122 children, in Harrow, England, reported a significant increase in lower respiratory tract infections in infants exposed to cigarette smoke. Colley et al[13] found that exposure to cigarette smoke in the first year of life doubled the risk of acquiring pneumonia or bronchitis. Also, there is ample evidence that later problems may occur. Leeder and colleagues[14] demonstrated that ventilatory function was impaired at age 5 years in children who had had pneumonia or bronchitis during their first year of

life. Dutau and Corberand[9] reported that apart from any infectious disease that can be passed to the infant by parents who smoke, passively inhaled cigarette smoke can lead to the development of chronic respiratory syndromes. Children in such families may become the future patients with chronic bronchitis.

Our study has demonstrated the adverse effect of passive inhalation of cigarette smoke during the first year of life. Although our data confirm the findings of others, previous reports have quantified lower respiratory infections from records of hospital admissions and/or parental questionnaries. These reports are based on selected populations with all the inherent biases of retrospective studies. In our study, the large number of patients enrolled, the prospective nature of the surveillance, and the in-office diagnosis by four trained physicians minimize such biases.

The effect of maternal smoking is striking and perhaps best explained by the fact that the mother, more often than the father, remained at home with the child. The incidence of "other" smokers in the household was infrequent and often included grandparents who lived with the family. The small number of other smokers in our study does not allow accurate statistical interpretation.

The significant difference in effects of the mother v the father smoking and the attendant respiratory problems in their children suggests that the duration of exposure to cigarette smoke, rather than the presence of a smoker in the house, is an important factor in infant-related respiratory disease. However, we failed to demonstrate a statistically significant relationship between the incidence of tracheitis and bronchitis and the number of cigarettes smoked. This failure may be the result of the large number of heavy smokers failing to specify the amount smoked. A surprisingly small number of mothers reported smoking more than one pack per day.

Leeder et al[16] have reported that a family history that is positive for chronic cough, asthma, and "wheezy bronchitis" placed infants at risk for the development of lower respiratory tract infections. Several studies[15,16] have shown that genetic factors associated with bronchitis and pneumonia in the first year of life may result in predisposition to wheezing in later childhood. Although much evidence suggests that genetic factors often are significant in the development of asthma and chronic bronchitis, damage to the airways caused by bronchitis and pneumonia in early childhood also may make children more susceptible to subsequent wheezing and/or chronic cough.[17] We have demonstrated a relationship between a family history that is positive for lower respiratory tract illness and the occurrence of bronchitis in infancy. A family history of both chronic cough and chronic bronchitis was positively correlated with an increased incidence of bronchitis in the infants studied. We were unable to distinguish between environmental and genetic factors influencing this association. From the results of our study and on the basis of the literature cited, we conclude that passive smoking is dangerous to the health of infants.

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Tominaga, S., Itoh, K. "Relationship between Parental Smoking and Respiratory Diseases of Three Year Old Children" Tokai J Exp Clin Med. 10(4): 395-399, 1985.

SUMMARY: In order to study the effect of the indoor pollution, particularly by parental smoking, on respiratory diseases of children, the relationship was examined between smoking by family members, use of various types of stoves and air conditioners, and the prevalence rate of respiratory disease in 7,916 three year old children who, for health check up, visited the Chita Public Health Center located in the Aichi Prefecture in 1976-1979.

Results of this study suggested that among various sources of indoor pollution, smoking by mother has the strongest effect on respiratory diseases, especially asthmatic bronchitis of young children, while the use of various types of stoves including non-ventilated keroshine [sic] stoves was not related significantly to the prevalence rate of respiratory diseases of those children except an increased rate of frequent common cold in children of households having an air conditioner(s).

Relationship between Parental Smoking and Respiratory Diseases of Three Year Old Children

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In order to study the effect of the indoor pollution, particularly by parental smoking, on respiratory diseases of children, the relationship was examined between smoking by family members, use of various types of stoves and air conditioners, and the prevalence rate of respiratory diseases in 7,916 three year old children who, for health check up, visited the Chita Public Health Center located in the Aichi Prefecture in 1978-1979.

Results of this study suggested that among various sources of the indoor pollution, smoking by mother had the strongest effect on respiratory diseases, especially asthmatic bronchitis of young children, while the use of various types of stoves including non-ventilated kerosine stove, was not related significantly to the prevalence rate of respiratory diseases of these children except an increased rate of frequent common cold in children of households having an air conditioner(s).

(Key Words: passive smoking, respiratory diseases, children, epidemiology, indoor pollution)

INTRODUCTION

Since Cameron reported a possible effect of parental smoking on respiratory diseases of children in 1969(2), a number of reports of epidemiological studies on the relationship between parental smoking and respiratory diseases have been reported (1, 3-11). In Japan Kasuga *et al* reported the results which suggested a synergistic effect of parental smoking and air pollution especially by exhaust gas of automobiles on the prevalence rate of respiratory symptoms in school children(6). Matsuki *et al* reported the results on the effect of passive smoking on the increased concentration of hydroxproline in the urine which could be an indication of increased destruction of collagen tissue in the lung(8). We also studied the relationship between parental smoking and other sources of indoor pollutions and the prevalence of respiratory diseases of 3 year old children who visited a public health center for health check up. The major results of this study are presented in this report.

MATERIALS AND METHODS

The study subjects are 7,916 three year old children who, for health check up visited the Chita Public Health Center located in Aichi Prefecture, in 1978-1979. This public health center serves three cities of Tokai, Chita and Tokoname with a total population of 215,802 in 1981 (Fig. 1). The total number of three year old children in the three cities in 1978-1979 was 8,060. The number of three year old children who visited the well being clinic at the Chita Public Health Center was 7,916 (98.2% of all three year old children). A standard questionnaire on the complaints of various symptoms has been routinely administered to all mothers and other guardians who accompanied children. Questions on smoking of family members and the use of various types of stoves and air conditioners were added to that standard questions

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in the study period of 1978–1979. The number of questionnaires available for analyses was 7,885.

Children with a possible respiratory disease were screened by the questionnaire and a physician at the public health center who makes a general health check up of all children. Those screened children with a possibility of some respiratory diseases are referred to the special clinic for respiratory diseases where a pediatrician who specializes respiratory diseases makes further examinations and gives a final diagnosis of respiratory diseases without knowing the information on the smoking status of family members and other sources of indoor pollution. The number of children who were screened for further respiratory examination was 462 (5.8% of all children who visited the public health center). Of those 462 children 431 children (93.3%) received further respiratory examinations at the special clinic. Their final diagnoses were bronchial asthma in 86 children (1.1%), asthmatic bronchitis* in 228 children (2.9%) and other respiratory diseases in 117 children (1.5%).

The prevalence rates of bronchial asthma and asthmatic bronchitis as well as frequent common cold (more than 5–6 times of catching a cold per year) which appears on the standard questionnaire were related to the smoking status of family members and the use of various types of stoves and air conditioners. The statistical significance was tested by using a chi-square test with a continuity correction.

RESULTS

The percentage of smokers in family members was 74.4% for fathers and 6.1% for mothers. The percentage of households having various types of stoves and room air conditioner was as follows: 78.4% for non-ventilated kerosine stove, 24.1% for electric stove, 10.2% for ventilated clean air type heater, 7.3% for gas stove and 52.2% for room air conditioner.

The prevalence rates of bronchial asthma, asthmatic bronchitis and frequent common cold in three year old children were compared according to the smoking status of the family members (Fig. 2).

The prevalence rate of bronchial asthma was

lower in children with smoking father or mother compared to that in children with no smoking members in the family. The difference was not statistically significant and this apparently paradoxical trend could be an indication that parents having a child with bronchial asthma may have been refrained from smoking. On the other hand, the prevalence rate of asthmatic bronchitis was higher in children with smoking father and/or mother. The prevalence rate of asthmatic bronchitis in children with a smoking mother was significantly higher than that in children with no smoking family members (4.9% vs. 2.3%. $p < 0.01$). The prevalence rate of frequent common cold was slightly higher in children with smoking father and/or mother. but the difference was not significant statistically. The prevalence rates of asthmatic bronchitis and frequent common cold in three year children were compared according to the use and non-use of various types of stoves and room air conditioners, but no significant differences were observed between families having and not having various types of stoves except the prevalence rate of frequent common cold was significantly higher in children of households having a room air conditioner(s) (Fig. 3). However, this excess rate of frequent common cold could be the results of lower room temperature rather than the excess indoor pollution caused by the use of air conditioner.

The prevalence rates of asthmatic bronchitis and frequent common cold in three year old children were further compared according to the smoking status of the family members and the use and non-use of various types of stoves and air conditioner. The effect of smoking by the family members seemed larger than the effect of indoor pollution by using various types of stoves and air conditioners, but all the differences were not significant statistically.

Finally, the prevalence rates of asthmatic bronchitis and frequent common cold were compared according to the smoking status of father and mother and the presence or absence of cough and sputum in family members (Fig. 4). The prevalence rate of asthmatic bronchitis in children with a smoking mother and the presence of family members with cough and sputum was unusually high which was signifi-

foot note: *the so-called "asthmatic bronchitis" is usually a recurrent bronchitis with moist low pitch wheeze.

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cant statistically compared to that in children with either one of smoking mother or family members with cough and sputum. There was a trend that the prevalence rate of frequent common cold was higher in children with family members with cough and sputum which could be an indication of infection from family members to children.

DISCUSSION

In this study three year old children were selected for the target subjects of passive smoking because those younger children were considered more sensitive to indoor pollution than older children and adults. From this study it was suggested that among various sources of indoor pollution, smoking by mother who contact her children closely for a long time had the strongest effect on respiratory diseases, especially asthmatic bronchitis of young children. In Japan the use of non-ventilated kerosine stove is regarded as a major source of the indoor air pollution at home, but the effect of the use of kerosin stoves on respiratory diseases of young children seemed much smaller than the effect of smoking by mother. The presence of family members with cough and sputum was related to the excess rate of asthmatic bronchitis which could also be an indication of results of smoking. The use of air conditioner was related positively to the rate of frequent common cold which could be an indication of maladaptation to low temperature in the room or change in temperature between indoor air and outdoor air.

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Aichi Prefecture
population : 6,265,118

Aichi Prefecture

Chita Public Health Center

City	Population	No. of Households
Tokai	95,517	29,564
Chita	66,289	17,954
Tokoname	53,996	14,370
Total	215,802	61,888
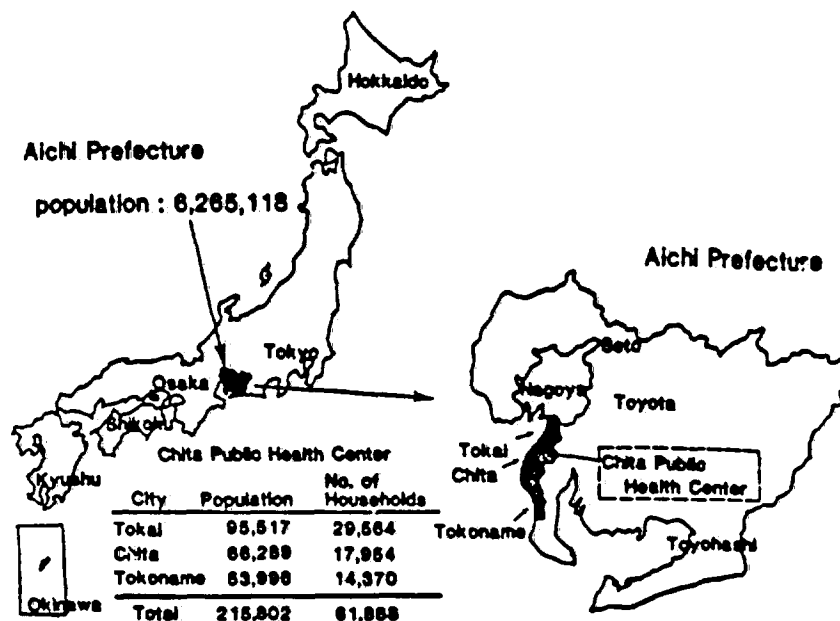
Fig. 1   Maps of the study area.

Bronchial asthma

Asthmatic bronchitis %

Frequent common cold (>5-6/year)

smoker   N F M   N F M   N F M

N : no family members smoke
F : father smokes
M : mother smokes

**p<0.01
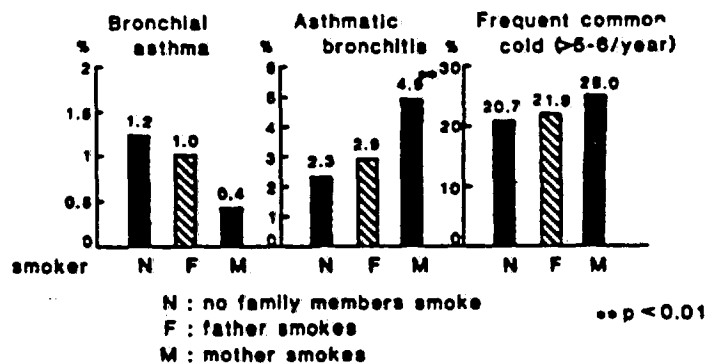
Fig. 2   Prevalence of respiratory diseases in three year old children according to the smoking habit of parents and other family members. Experience at the Chita Public Health Center.

Asthmatic bronchitis

Frequent common colds

use
Air
conditioner
Kerosine
stove
Gas
stove
Electric
stove
Ventilated
heater

• – : non-use   •• p(0.0)
• : use

Fig. 3   Prevalence of respiratory diseases in three year old children according to the use or non-use of air conditioner and various types of stoves.
Experience at the Chita Public Health Center.

Asthmatic bronchitis

Frequent common cold

cough
sputum
smoking
cigarettes   0   1-9   20-29 30   0   >1
                      father   mother

• p<0.05   ••• p<0.001
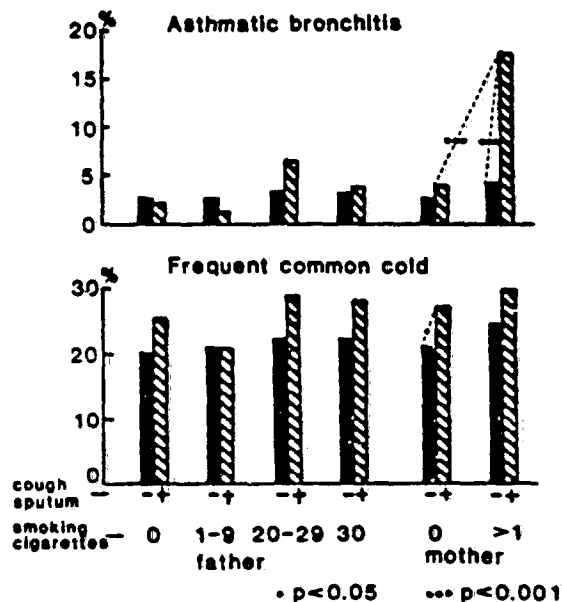
Fig. 4   Prevalence of respiratory diseases in three year old children according to the presence or absence of family members with cough and/or sputum and smoking habit of father and mother.
Experience at the Chita Public Health Center.

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Watkins, C.J., Sittampalam, Y., Morrell, D.C., Leeder, S.R.,
Tritton, E. "Patterns of respiratory illness in the first year of
life" British Medical Journal 293:794-796, 1986.

ABSTRACT: This paper describes a study of respiratory
illness during the first year of life in a cohort of infants who
were born between 1975 and 1978 to mothers who were registered
with two inner London group general practices. The types of
respiratory illness and their relation to the season of the year
and season of birth of the child are examined. The relations among
the frequency and type of respiratory illness and several social
and family factors that have previously been shown to be associated
with high levels of respiratory morbidity are also described.

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British Medical Journal VOLUME 293 27 SEPTEMBER 1986

Practice Research

Patterns of respiratory illness in the first year of life

C J WATKINS, Y SITTAMPALAM, D C MORRELL, S R LEEDER, E TRITTON

Abstract

This paper describes a study of respiratory illness during the first year of life in a cohort of infants who were born between 1975 and 1978 to mothers who were registered with two inner London group general practices. The types of respiratory illness and their relation to the season of the year and manner of birth of the child are examined. The relation among the frequency and type of respiratory illness and several social and family factors that have previously been shown to be associated with high levels of respiratory morbidity are also described.

Introduction

An association between various personal and family factors and an increased respiratory morbidity in children has been identified. These community surveys have relied on the mothers' responses to questionnaires at interview about their infants' health to estimate the occurrence of respiratory illness. Such estimates have disagreed substantially with estimates derived from direct studies of respiratory illness in patients who have presented to attending general practitioners. ...

Most serious respiratory illness in infancy is managed by general practitioners. Apart from the need for accurate diagnosis and effective treatment for the acute illness, the problem for the attending general practitioner is to identify and treat appropriately ...

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(left column — rotated text)

Details of self help groups are included in the newsletter. Usually between four and six group functions in the practice at one time. These have included relaxation, yoga (for men, first time mothers, parents of teenagers, and groups for those who wish to lose weight or give up smoking). The newsletter also contains items of health information—for instance, on hypothermia, flu jabs, taking your temperature, food labelling, and immunisation for holidays. Other items have included news of staff changes, book reviews, articles on the history of the practice, details of fundraising events held by the Practice Participation Association, and local issues related to health.

The newsletter covers (four sides of A4 paper). A typical front page is shown in the figure.

How is the newsletter distributed?

During 1982 the practice register was arranged geographically by volunteers to create a street index. It is thus possible to identify patients who live in a household, and labels are printed with the names of individual patients, one label per household. The task of reorganising the practice register of 11 500 patients geographically would probably occupy a full time person for about three weeks.

Two voluntary managers organise the distribution of newsletters to individual households. One hundred and twenty volunteers have been recruited by advertisements in the newsletter and in the surgery. Most deliver 50 to 100 newsletters in a geographically limited area, usually near their homes. To meet the requirements of the local medical committee that the newsletter should not be construed as advertising for the practice, each newsletter is folded in three, leaving the outside largely blank, and sealed with an address label.

The cost of producing each edition of the newsletter is approximately £150. This is met by the association, which has a successful fundraising group. The cost is low only because of the enormous amount of voluntary help offered by members of the practice. The self adhesive address labels cost £45 to produce for each edition, and this is met by the practice—the only cost to the doctor of the newsletter.

What does the newsletter achieve?

To assess what impact the newsletter has on members of the practice, a survey was carried out of patients' views of the newsletter. 178 patients who attended one of the surgeries and 42 patients who attended an open meeting of the association completed a questionnaire. Of these patients, 78% had heard of *Working Well*, most of whom knew that it was the newsletter of the practice association; 65% had read the last issue, though only 42% could remember a specific item in the last issue. Few patients made negative comments about the newsletter in the questionnaire, and no one has ever asked to be excluded from the delivery list.

There have been few spontaneous contributions from patients, but many people tell the deliverers that they welcome the newsletter, and several new patients have said how impressed they were by this evidence of community feeling in the practice. Delivering the newsletter is a simple task, and many people seem to enjoy having the opportunity to give something back to the practice in this way. Several have become group leaders or fundraisers, and the newsletter clearly performs an important recruiting role for the Practice Participation Association.

Conclusion

The practice newsletter has been produced regularly for three years with voluntary help, and thus the cost can be supported by the Practice Participation Association. Delivering it to households provides an unusual way of informing all members of the practice of the association's activities. It is hoped that the newsletter helps to promote a feeling among patients that they belong to a practice "community".

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immediately after birth. By the time they are exposed in the second winter their defence mechanisms have matured sufficiently to protect them from infection. The role of immunity can be clarified only when simple methods of identifying viruses and of measuring the immune status of children become available for use in general practice. Studies carried out in hospital are unlikely to be helpful—only three of the 404 children in our study were admitted to hospital.

In this study the role of family health and social variables is not as clear cut as that reported by Leeder *et al.* The striking finding in this study is the social class difference in frequency of consultation for respiratory illness, with high consultation rates for those whose fathers were in manual occupations. This is not explained by the fact that the families from which such children come are more likely...

TABLE I—*Experience of respiratory illness reported by the general practitioner as a birth cohort of 404 children*

TABLE II—*Relations between several social and family factors and the attack rate of lower respiratory illness per 100 children per year presented as a birth cohort of 404 children*

Discussion

Because of the wide interdoctor variation in the diagnosis of respiratory illness in the winter months, and in particular the peak of incidence of lower respiratory illness occurring in the month of February, strongly suggest infection...

We thank the parents and the doctors of the Lambeth Road Group Practice and the Linton Road Group Practice for providing the data for this study. Miss Mary Evans, Mr George Penman, and Mr Clive Murray for their help in data collection. Professor W W Holland, Professor J Horne, Dr M Pollock, and Mr D Shannon for their expert guidance on the design of the study, members of the department of community medicine for their comments on earlier drafts of this paper, and Mrs Carmel Stephenson for patiently typing many drafts of this paper. The study was supported in part with a grant from the Department of Health and Social Security.

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Burchfiel, C.M., Higgins, M.W., Keller, J.B., Howatt, W.F., Butler,
W.J., Higgins, I.T.T. "Passive Smoking in Childhood: Respiratory
Conditions and Pulmonary Function in Tecumseh, Michigan" Am Rev
Respir Dis 133: 966-973, 1986.

ABSTRACT. The relationship of passive smoking to respiratory
conditions and pulmonary function was assessed using a cross-
sectional design in the defined population of Tecumseh, Michigan.
The study population was made up of 3,482 children who were 0 to
19 yr of age at the 1962-1965 examination and for whom questionnaire
information was available for both parents. Nearly 62% of children
in this age group were exposed at the time of examination to at
least 1 parent who smoked. Passive exposure to cigarette smoke
was associated with an elevated prevalence of phlegm, wheeze,
asthma, and chest colds among males and wheeze, bronchitis, and
chest colds among females. Using logistic regression, offspring
were shown to be 1.5 to 2.0 times more likely to have a respiratory
condition if both their parents currently smoked than if both
parents never smoked. FEV_1 and FVC among males and Vmax50 among
females were significantly lower by 5% in nonsmokers 10 to 19 yr
of age whose parents were current smokers compared with similar
offspring of never smoking parents. Respiratory conditions were
generally more frequent and the level of lung function was generally
lower for males from households where only mothers smoked compared
with males from households where only fathers smoked, although
sample size was limited. In females similar relationships were
less consistent. Differences tended to be larger and more often
significant for males than for females when respiratory symptoms
and illness were examined. Comparisons between offspring of 2
current and 2 never smoking parents and those involving the number
of parental smokers in a child's lifetime provided stronger
associations of passive smoking with respiratory conditions and
lung function than did the number of household smokers, duration,
or amount of parental smoking. In general, these associations
were independent of parental education, family size, parental
reporting bias, and the child's own smoking habits.

Passive Smoking in Childhood

Respiratory Conditions and Pulmonary Function In Tecumseh, Michigan[1-4]

CECIL M. BURCHFIEL, MILLICENT W. HIGGINS, JACOB B. KELLER, WILLIAM F. HOWATT, WILLIAM J. BUTLER, and IAN T. T. HIGGINS

Introduction

Until recently, relatively few studies have focused on the health effects of passive or involuntary smoking. Passive smoking during infancy and childhood has been associated with acute respiratory illness (1-16), chronic respiratory symptoms (17-22), and reduced pulmonary function (21, 23-26), although not all investigations have confirmed these associations (27-31). The qualitative and quantitative differences of mainstream and sidestream cigarette smoke have been documented (32, 33); a number of constituents are more concentrated in sidestream than in mainstream smoke. The need for better characterization of exposure and control of potential confounding factors has been recognized (34-37).

Investigations involving young children are of interest for several reasons: (1) confounding effects of active smoking and occupational exposures are absent, (2) children may be more exposed and/or susceptible than adults, and (3) the risks of passive exposure can be assessed during the period of lung growth and development. Children spend 60 to 80% of their time indoors (38), depending on season and geographic location. Because cigarette smoking is prevalent among adults, the likelihood of passive exposure in children is high. It has been estimated that 54 to 70% of children are exposed to one or more cigarette smokers in the household environment (1, 27, 28, 38, 39). Because of the large number of exposed persons, the proportion of time spent indoors and recent energy conservation efforts, the public health impact of passive smoking could be substantial.

The purpose of this study was to assess the cross-sectional relationships of passive smoking to respiratory symptoms, illnesses, and lung function in children and adolescents of Tecumseh, Mich-

igan. Several measures of passive smoking were developed from questionnaire data. Effects of parental education, family size, parental symptoms and illnesses, and active smoking by the children themselves are evaluated.

Methods

Study Population

Residents of Tecumseh, Michigan have been participants in a community-based prospective investigation for the past 25 yr. The major purpose of the Tecumseh Community Health Study has been to identify determinants of health and disease in a natural community. Its design, methods, and historical perspective have been described previously (40-42). Standard questionnaires, certain physiologic measurements, and clinical assessments by physicians were available.

During the second cycle of examinations, conducted between 1962 and 1965, a total of 4,378 children and adolescents 0 to 19 yr of age were interviewed and examined. Of the

4,378 subjects, the following were excluded from this investigation: 82 because they were not residing with their parents, 688 because both parents were not interviewed, and 126 because they were active smokers (smoking habits were available only for those 16 to 19 yr of age; children 15 yr of age or younger were assumed to be nonsmokers). A total of 3,482 nonsmoking males and females 0 to 19

SUMMARY The relationship of passive smoking to respiratory conditions and pulmonary function was assessed using a cross-sectional design in the defined population of Tecumseh, Michigan. The study population was made up of 3,482 children who were 0 to 19 yr of age at the 1962-1965 examination and for whom questionnaire information was available for both parents. Nearly 82% of children in this age group were exposed at the time of examination to at least 1 parent who smoked. Passive exposure to cigarette smoke was associated with an elevated prevalence of phlegm, wheeze, asthma, and chest colds among males and wheeze, bronchitis, and chest colds among females. Using logistic regression, offspring were shown to be 1.5 to 2.0 times more likely to have a respiratory condition if both their parents currently smoked than if both parents never smoked. FEV$_1$ and FVC among males and Vmax$_{50}$ among females were significantly lower by 5% in nonsmokers 10 to 19 yr of age whose parents were current smokers compared with similar offspring of never smoking parents. Respiratory conditions were generally more frequent and the level of lung function was generally lower for males from households where only mothers smoked compared with males from households where only fathers smoked, although sample size was limited. In females similar relationships were less consistent. Differences tended to be larger and more often significant for males than for females when respiratory symptoms and illnesses were examined. Comparisons between offspring of 2 current and 2 never smoking parents and those involving the number of parental smokers in a child's lifetime provided stronger associations of passive smoking with respiratory conditions and lung function than did the number of household smokers, duration, or amount of parental smoking. In general, these associations were independent of parental education, family size, parental reporting bias, and the child's own smoking habits.

AM REV RESPIR DIS 1986; 133:966-973

yr of age and members of their households constituted the study population.

Questionnaire

Personal, demographic, and medical information were ascertained using a standard questionnaire. Parents responded for children 15 yr of age or younger. Several respiratory symptoms and illnesses were selected for evaluation: these included cough, phlegm, wheeze, asthma, bronchitis, and colds settling in the chest. In general, questions involved a past history of these conditions, rather than ascertainment of symptoms and illnesses defined only at the time of interview. Specific questions used to define these respiratory conditions and results concerning neonatal, allergic, and other conditions are reported elsewhere (43). The diagnostic criteria for asthma, reported by Higgins and Keller (44) and Broder and coworkers (45), were used, and a probable or suspect diagnosis was included as asthma.

Information was available concerning parental education, family size, and presence or absence of parental respiratory symptoms or illness. Categories of parental education included: (1) at least one parent who did not complete high school, (2) both parents completed high school, and (3) either parent attended college. Family size was defined as the number of persons residing in a household. Categorical definitions were used to classify children according to whether their mothers or fathers had a history or diagnosis of the specific respiratory condition under study.

Pulmonary Function

A Wedge® spirometer (Med-Science Electronics, Burlington, MA) and a two-channel recorder (Sanborn Co., Waltham, MA) operating at a paper speed of 25 mm/s were used to measure lung function. Following maximal inspiration, subjects performed several maximal expiratory efforts until 2 satisfactory tracings were obtained. Measurements of volume and flow were based on the tracing with the largest vital capacity and were adjusted to body temperature and pressure saturated with water vapor (BTPS).

Seven volume and flow measurements were available (46); forced expiratory volume in one second (FEV_1), forced vital capacity (FVC), and forced expiratory flow at 50% of vital capacity ($Vmax_{50}$) were selected for use in this study because they have been used in other studies and were available at subsequent examinations. Lung function analyses reported here involved young persons 10 to 19 yr of age in 1962 through 1965.

Measures of Passive Smoking

Children were classified by smoking habits of their household members at the time of interview. Only cigarette smoking and not pipe or cigar smoking was taken into account. Five measures of passive smoking were developed.
I. Current and Past Parental Smoking Habits:

| Father: | Never | Current | Current | Never | All |
| Mother: | Never | Current | Never | Current | Others |

II. Number of Parental Smokers During Child's Lifetime: (0, 1, and 2).
III. Number of Current Household Smokers: (0, 1, 2, 3, or more).
IV. Duration of Parental Smoking During Child's Lifetime.
V. Current Amount of Parental Smoking.

The first index provided one of the more extreme contrasts in passive smoke exposure, where children having both parents who never smoked are compared with those having both parents who were current smokers. Children from households where only fathers smoked and where only mothers smoked could also be compared using this index. The "all others" category included children having one or both parents who were former smokers. For the second index, children were categorized by presence or absence of parental smoking during the child's lifetime. To include potential prenatal exposure to parental smoking, a child's lifetime was defined as 1 yr before birth to the time of examination in 1962-1965. Smoking habits of siblings and relatives who were 16 yr of age or older were included with those of parents in the classification of current household smokers. For duration and amount of parental smoking, the number of years and average number of cigarettes smoked per day by each parent were summed.

Data Analysis

Prevalence rates of respiratory symptoms and illnesses, and levels of lung function in children and adolescents were compared across parental smoking categories using 5-yr, age- and sex-specific groups. Stratification was used initially to control for potential confounding by parental education, family size, parental history of respiratory symptoms or illness, and active smoking by adolescents. Significance was assessed using standard t and chi-square tests for differences between means and proportions, respectively. Age-adjusted prevalence rates were derived using the age distribution of all nonsmoking subjects 0 to 19 yr of age examined in 1962-1965 as a standard. A Cochran/Mantel-Haenszel procedure was used to test for the average partial association between passive smoking and a specific respiratory symptom or illness, controlling for the effects of age group and assessing whether a linear trend exists (47). To compare age-adjusted means, variances for those having or not having a specific respiratory condition were calculated, and a standard z statistic for comparing means with known but unequal variances was used to determine significance.

Multiple logistic regression (48) was employed to control for potential confounders simultaneously. Sex-specific analyses were performed using each respiratory condition as the response variable. The number of parental smokers during a child's lifetime (0, 1, 2) was selected as the independent variable of primary interest and was coded using 2 indicator variables. Parental education, family size, parental symptom or illness, as well as age of the child were considered as covariates. For asthma a diagnosis of hay fever and history of other allergies were also included in the model as potential predictors. Several methods of including age were considered; regression coefficients were similar for each. Likelihood ratio tests (48) were used to compare methods of including age, to decide whether certain variables should be retained in the logistic model, and to confirm whether or not statistical interaction was present. Goodness of fit for these logistic models was assessed using methods proposed by Lemeshow and Hosmer (49), where information from both cases and noncases is incorporated.

Levels of lung function were expressed as a percent of predicted or were adjusted using analysis of covariance. Predicted values of FEV_1, FVC, and $Vmax_{50}$ were obtained by regressing observed values of asymptomatic nonsmokers on age and height separately for 2 age and sex groups using the population of nonsmokers 10 to 19 yr of age who were

TABLE 1

REGRESSION STATISTICS FOR LUNG FUNCTION MEASUREMENTS, ASYMPTOMATIC NONSMOKING MALES AND FEMALES, TECUMSEH, 1962-1965*

Sex	Age (yr)	Measure	Regression Statistics					
			n	a	b_1	b_2	R^2	Sy·x
Male	10-15	FEV_1	528	-5.293	0.115	0.043	0.747	0.423
		FVC	528	-6.447	0.118	0.052	0.739	0.507
		$Vmax_{50}$	516	-4.311	0.152	0.036	0.490	0.729
	16-19	FEV_1	127	-3.722	-	0.046	0.269	0.534
		FVC	127	-5.214	-	0.064	0.303	0.720
		$Vmax_{50}$	124	-1.226	-	0.034	0.075	0.890
Female	10-15	FEV_1	524	-3.688	0.093	0.032	0.550	0.396
		FVC	524	-4.322	0.096	0.038	0.559	0.437
		$Vmax_{50}$	514	-2.816	0.112	0.031	0.264	0.754
	16-19	FEV_1	155	-3.397	-	0.040	0.233	0.432
		FVC	155	-3.305	-	0.041	0.220	0.459
		$Vmax_{50}$	154	-2.134	-	0.037	0.054	0.940

* Regression model: Predicted lung function = $a + b_1 \cdot$ age (yr) $+ b_2$ (height in cm) for 10- to 15-yr-olds; predicted lung function = $a + b_2 \cdot$ height (cm) for 16- to 19-yr-olds.

TABLE 2

PREVALENCE OF PARENTAL SMOKING AMONG
SUBJECTS 0 TO 19 YR OF AGE, TECUMSEH,
1962-1965

Parental Smoking			
Father	Mother	n	%
Never	Never	567	15.7
Current	Current	1,136	31.5
Current	Never	983	27.2
Never	Current	109	3.0
All others		813	22.5
Total		3,608	99.9

free of asthma and wheeze without colds, and if 16 to 19 yr of age, free of cough, phlegm, and moderate or severe shortness of breath. A total of 1,357 nonsmokers 10 to 19 yr of age met these criteria and had complete age, height, and lung function data (FEV_1, FVC, or $Vmax_{50}$). The significant terms of the selected regression model included age and height for those 10 to 15 yr of age and height only for those 16 to 19 yr of age. Regression statistics for these models are presented in table 1. Models that included powers of height, weight, or interaction terms did not increase substantially the amount of variation explained by the simple model employing only age and height. Race was not included in the models because all subjects are white. Regression statistics for FEV_1 and $Vmax_{50}$ were published previously for nearly the same group of children 10 to 15 yr of age (50). Sex-specific regressions were used because of differences between males and females in lung growth.

Analysis of covariance models were also used to adjust levels of lung function for age and height, parental education, and family size (51). The covariance model assumes no interaction and a linear relationship between covariates and lung function. Tests for equality of slopes among those exposed and unexposed to parental smoking were performed to rule out interaction; linearity was also assessed. Both assumptions for the model were met (43). In contrast to the percent of predicted method of adjustment, this approach does not require definition of a healthy

standard population and allows comparisons to be made in units of actual lung volume or flow.

Results

Prevalence of Passive Smoking
Prevalence of passive exposure to cigarette smoke was estimated using two-parent households where both parents were interviewed (table 2). A total of 61.7% of all subjects 0 to 19 yr of age had at least one currently smoking parent; 31.5% had both parents who currently smoked. Having a father as the only parental smoker was far more prevalent than having a mother as the only parental smoker (27.2% versus 3.0%). Only 15.7% of the subjects 0 to 19 yr of age were never exposed to parental smoking.

Respiratory Symptom and Illness Prevalence
Prevalence rates of several respiratory symptoms and illnesses in Tecumseh have been shown previously to vary with age and sex (43). Age-specific prevalence rates of several respiratory conditions are presented in table 3. For most respiratory conditions, prevalence rates tended to be higher in males than in females, significantly so for phlegm, wheeze, asthma, and chest colds in at least one of the age groups. Cross-sectional frequencies of phlegm, wheeze, and chest colds tend to decrease as age increases, whereas with cough, asthma and bronchitis prevalence rates vary with age in a less consistent manner. Age-adjusted prevalence rates of 4 respiratory conditions are presented by parental smoking category for males and females in figures 1 and 2, respectively. For both sexes and all 4 conditions, prevalence rates were higher among nonsmoking children whose parents both currently smoked than among children whose parents never smoked. Differences
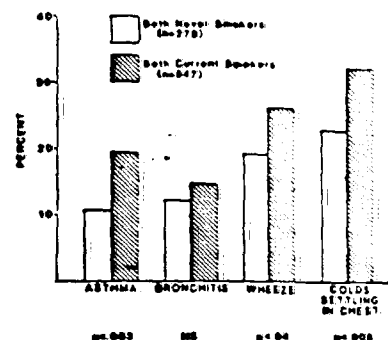

Fig 1. Age-adjusted prevalence of respiratory conditions by parental smoking, male nonsmokers 0 to 19 yr of age, Tecumseh, 1962-1965.

were significant for the majority of conditions.

When the number of parental smokers during a child's lifetime was considered, age-adjusted prevalence rates were highest for children exposed to 2 parental smokers and generally lowest for unexposed children, the trend being significant for phlegm, wheeze, asthma, and colds settling in the chest among males and for wheeze, bronchitis, and colds settling in the chest among females (table 4). Although not presented in detail here, for all respiratory conditions except bronchitis in males, parents of nonsmokers 0 to 19 yr of age reported smoking significantly more cigarettes (mean differences ranged from 1 to 4 per day) and for significantly longer periods of time (mean differences ranged from 7 to 24 months) when a given respiratory symptom or illness was reported for their children than when it was not reported, after adjusting for differences in age ($p < 0.0001$).

Previous work in Tecumseh has shown that parental smoking habits are related to parental education but not to family size (43, 52). In this investigation, level of education was highest among households where both parents never smoked. Although not shown here, children from households where both parents currently smoked tended to have higher respiratory symptom and illness prevalence rates than those where both parents never smoked within each degree of parental education and family size.

When results were stratified by parental history of a given respiratory condition, there was some reduction in the magnitude of the parental smoking effect, yet for several conditions the relationship remained significant. For example, in households where both parents

TABLE 3

PREVALENCE (%) OF RESPIRATORY SYMPTOMS AND ILLNESSES BY AGE AND SEX, NONSMOKING
CHILDREN FROM TWO-PARENT HOUSEHOLDS, TECUMSEH, 1962-1965*

Respiratory Condition	0-4		5-9		10-14		15-19	
	M (n = 470)	F (n = 491)	M (n = 555)	F (n = 540)	M (n = 482)	F (n = 480)	M (n = 241)	F (n = 243)
Cough	7.6	8.6	10.7	9.5	10.8	7.6	7.3	7.8
Phlegm	18.4	13.5†	14.1	14.9	13.7	9.7	8.5	8.9
Wheeze	31.7	24.9†	20.6	18.5	19.5	15.0	17.9	16.2
Asthma	13.6	10.7	16.2	9.2§	17.0	9.7‡	13.3	8.2
Bronchitis	13.3	10.5	15.9	12.6	11.0	10.0	11.7	14.5
Chest cold	39.9	30.4‡	29.4	28.5	20.9	19.0	19.2	14.9

* Differences tested between males and females within each age group using chi-square.
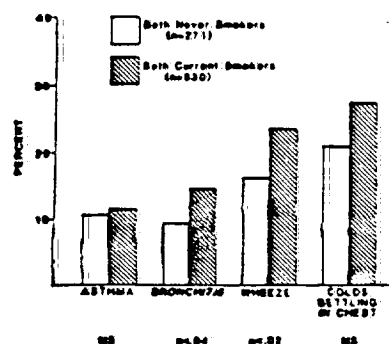† $p < 0.05$.
‡ $p < 0.01$.
§ $p < 0.001$.

Fig. 2. Age-adjusted prevalence of respiratory conditions by parental smoking, female nonsmokers 0 to 19 yr of age, Tecumseh, 1962-1965.

reported a history of phlegm, male offspring had a prevalence rate for phlegm of 13.4, 12.5, and 18.5% for 0, 1, and 2 parental smokers, whereas the prevalence rate was 14.9, 9.0, and 17.5%, respectively, when both parents denied history of phlegm. Differences remained significant for phlegm and asthma among males regardless of a history of the same symptom or illness in their parents.

Results obtained using logistic regression models are presented in table 5. The odds ratios represent measures of the degree of association between passive smoking and each respiratory condition controlling for potential confounding by age, parental education, and family size. For example, the odds of a male 0 to 19 yr of age having asthma are 2.16 times as great if he was passively exposed to 2 parents who currently smoked than if he was unexposed. For both sexes and almost all respiratory conditions, odds ratios were higher for children with 2 parental smokers compared with children who had never been exposed to parental cigarette smoke. Odds ratios tended to be higher for males from households where mothers were the only smokers than for males from households where only fathers smoked. The pattern was reversed, though less consistently, for females.

When logistic regression models employing the number of parental smokers during a child's lifetime (0, 1, or 2) were used as a measure of passive smoking, similar odds ratios were obtained for most respiratory conditions. When children with one parental smoker were compared with the unexposed reference group, odds ratios were frequently close to or less than 1.0, yet did not differ significantly from 1.0. This suggests that exposure to one parental smoker, who was

most often the father, is not associated with an increased probability of having these respiratory symptoms or illnesses. In comparing logistic models using the 2 different passive smoking measures, the -2 log likelihood values and the fraction of variance explained by the models are almost identical, suggesting that little is gained statistically by categorizing parental smoking more completely with 5 as opposed to 3 levels (43). An analysis of the goodness of fit for these logistic models revealed close agreement between observed and expected cases across deciles of risk.

Pulmonary Function

Mean lung function expressed as a percent of predicted is presented in figure 3 for nonsmoking males and females 10 to 19 yr of age whose parents were both

never (98 males and 93 females) or current (201 males and 199 females) smokers. Mean FEV_1 and FVC for males and $Vmax_{50}$ for females were significantly lower if both parents were current smokers rather than never smokers. Results were virtually identical when 10- to 14- and 15- to 19-yr-old age groups were analyzed separately.

Levels of FEV_1 and FVC for males and $Vmax_{50}$ for females were inversely related to the number of parental smokers during a child's lifetime among nonsmokers 10 to 19 yr of age. Using analysis of covariance to adjust levels of lung function for age and height, male nonsmokers 10 to 19 yr of age from households where both parents smoked had a mean FEV_1 that was 144 ml (4.6%) lower than that for males with no parental smokers (table 6). Similarly, a deficit of 173 ml (4.9%) in

TABLE 4

AGE-ADJUSTED PREVALENCE (%) OF RESPIRATORY CONDITIONS BY SEX AND NUMBER OF PARENTAL SMOKERS DURING CHILD'S LIFETIME, NONSMOKERS 0 TO 19 YR OF AGE, TECUMSEH, 1962-1965*

	Males			Females		
	Number of Parental Smokers			Number of Parental Smokers		
Respiratory Condition	0 (n = 339)	1 (n = 718)	2 (n = 681)	0 (n = 360)	1 (n = 716)	2 (n = 648)
Cough	8.6	8.4	11.4	8.4	8.0	8.7
Phlegm	13.4	12.8	18.8†	8.7	13.5	13.6
Wheeze	20.9	20.4	26.5†	16.0	17.3	22.9‡
Asthma	13.4	11.3	20.9§	9.8	7.9	11.7
Bronchitis	12.0	11.9	15.2	8.8	11.3	13.2†
Chest cold	23.4	27.6	32.0‡	20.0	22.4	27.4‡

* Generalized Cochran/Mantel-Haenszel test for average association in three-way contingency tables
† p < 0.05
‡ p < 0.01
§ p < 0.001.

TABLE 5

ODDS RATIOS RELATING PARENTAL SMOKING TO RESPIRATORY CONDITIONS ADJUSTING FOR THIRD VARIABLES USING MULTIPLE LOGISTIC REGRESSION, NONSMOKING MALES AND FEMALES 0 TO 19 YR OF AGE, TECUMSEH, 1962-1965*†

		Parental Smoking				
Sex	Respiratory Condition	Father: Never Mother: Never	Current Current	Current Never	Never Current	All Others
Male	Cough	1.0	1.38	0.89	0.66	1.20
	Phlegm	1.0	1.62‡	0.83	1.77	1.15
	Wheeze	1.0	1.47‡	1.04	1.42	1.21
	Asthma	1.0	2.16‡	0.84	1.37	1.19
	Bronchitis	1.0	1.23	0.88	1.46	1.03
	Chest cold	1.0	1.56‡	1.16	1.30	1.37
Female	Cough	1.0	1.17	1.06	0.95	1.30
	Phlegm	1.0	1.43	1.92‡	0.81	1.44
	Wheeze	1.0	1.60‡	1.01	1.41	1.10
	Asthma	1.0	1.05	0.65	1.16	0.79
	Bronchitis	1.0	1.75‡	1.61	0.73	0.74
	Chest cold	1.0	1.39	1.19	0.90	1.00

* Odds ratios are relative to the reference category where both parents were never smokers
† Third variables include age, parental education, and family size for all except asthma where age, hay fever, and other allergies were used.
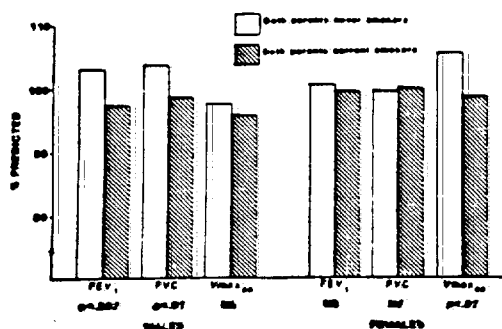‡ Significant at p < 0.05.

Fig. 3. Mean % predicted lung function by parental smoking; male and female nonsmokers 10 to 19 yr of age, Tecumseh, 1962–1965.

FVC for males 10 to 19 yr of age and of 185 ml/s (5.1%) in $\dot{V}max_{50}$ for females 10 to 19 yr of age was observed.

Although not presented here, mean level of lung function tended to be inversely related to the total number of smokers in the household; this was most evident for FEV_1% predicted among male nonsmokers, yet sample size was small, and trends were not significant (43). Lung function was also inversely related to duration and amount of parental smoking among nonsmoking males 10 to 19 yr of age but not among females (43).

Differences in lung function across parental smoking categories were similar in magnitude when results were stratified across levels of parental education and family size. When each potential confounder was included in an analysis of covariance, model associations between passive smoking and impaired lung function persisted.

Discussion

Prevalence rates of respiratory conditions and level of lung function have been examined in a defined community for nearly 3,500 young persons in relation to the smoking habits of their parents. The prevalence of passive exposure to cigarette smoke in Tecumseh during the 1962–1965 time period was similar to that found in other population surveys (1, 27, 39). Approximately 62% of those 0 to 19 yr of age in this study had at least one parent who currently smoked compared with 54 to 70% reported in other studies. Given the large proportion of children exposed, the amount of time spent indoors, especially by younger age groups, and recent energy conservation efforts, which reduce ventilation, the public health impact of passive smoking could be substantial.

Several indirect measures of passive exposure to household cigarette smoke were developed from questionnaire data. Most investigations to date have used either a dichotomous classification or the number of current parental smokers as exposure variables; only one study defined exposure to parental smoking with reference to the child's lifetime (25). A few studies have classified exposure based on the number of cigarettes currently smoked per day (5, 9, 18, 53). Although results of this investigation were generally similar for all measures of passive smoking, current and past smoking habits and the number of parental smokers during a child's lifetime were most useful in assessing passive smoking and respiratory outcomes. Misclassification of exposure was a potential problem both for this investigation and others preceding it. The frequency of contact between children and their parents while cigarette smoking occurred, as well as exposure patterns in day care settings for young children of working parents, are additional factors that should be addressed in future research.

Passive exposure to cigarette smoke was associated with increased prevalence of phlegm, wheeze, asthma, and colds settling in the chest among males, and wheeze, bronchitis, and colds settling in the chest among females in Tecumseh. Several cross-sectional studies have demonstrated significant associations between parental smoking and phlegm (17), wheeze (17, 21), bronchitis (5–7), and asthma (12, 15), whereas others have not documented such associations (16, 27). The lack of significant association between parental smoking and history of cough in this study was consistent with results of several studies (16, 27) but not with those of others (17–19, 22). Cameron and Robertson (4) were among the first to suggest that differences in illness prevalence related to parental smoking might be of greater magnitude in geographic locations where more time is spent indoors because of the climate.

The significant inverse relationship observed in this investigation between parental smoking and level of lung function in nonsmokers 10 to 19 yr of age is consistent with several previous studies (21, 23–26, 54) but not with others (17, 27, 28, 30). Most of the studies showing a positive association also demonstrated a dose-response relationship. Results of

TABLE 6

MEAN (± SE) LUNG FUNCTION IN CHILDREN ADJUSTED FOR AGE AND/OR HEIGHT USING ANALYSIS OF COVARIANCE BY NUMBER OF PARENTAL SMOKERS, TECUMSEH, 1962–1965*

Sex	Age (yr)	Parental Smokers (n)	Examined (n)	FEV_1 (L)	FVC (L)	$Vmax_{50}$ (L/s)
Male	10–14	0	70	2.812 ± 0.047	2.924 ± 0.055	3.105 ± 0.083
		1	197	2.582 ± 0.028	2.875 ± 0.033	3.227 ± 0.049
		2	180	2.480 ± 0.030	2.790 ± 0.034†	3.060 ± 0.057
	15–19	0	41	4.210 ± 0.084	4.341 ± 0.108	4.866 ± 0.141
		1	106	4.067 ± 0.052	4.343 ± 0.067	4.811 ± 0.088
		2	75	4.052 ± 0.062	4.328 ± 0.080	4.499 ± 0.105
	10–19	0	111	3.139 ± 0.043	3.565 ± 0.053	3.826 ± 0.074
		1	303	3.080 ± 0.026	3.466 ± 0.032	3.686 ± 0.045
		2	255	2.995 ± 0.028‡	3.392 ± 0.035‡	3.537 ± 0.049
Female	10–14	0	85	2.373 ± 0.048	2.579 ± 0.053	3.365 ± 0.094
		1	181	2.380 ± 0.028	2.563 ± 0.032	3.238 ± 0.056
		2	169	2.368 ± 0.029	2.591 ± 0.033	3.187 ± 0.058
	15–19	0	50	3.041 ± 0.057	3.267 ± 0.062	4.074 ± 0.127
		1	109	3.003 ± 0.039	3.246 ± 0.042	3.852 ± 0.086
		2	72	3.039 ± 0.048	3.285 ± 0.051	3.853 ± 0.106
	10–19	0	115	2.807 ± 0.037	2.818 ± 0.040	3.614 ± 0.076
		1	290	2.802 ± 0.023	2.826 ± 0.025	3.457 ± 0.048
		2	241	2.809 ± 0.025	2.835 ± 0.028	3.429 ± 0.052†

* Defined during child's lifetime excluding smokers 16 to 19 yr of age
† $p < 0.05$
‡ $p < 0.01$

this research tend to support these findings for several measures of lung function, although the minimal level at which an effect of parental smoking can be detected remains unclear. Investigators have suggested that the lack of association observed in several studies may be due to climatic factors (17, 27), selection of a pulmonary function measure (peak expiratory flow), which may not be adequately sensitive (30), or small sample size (55). Schilling and coworkers (28) did not show a significant relationship in general, although significantly lower maximal flow at 50% of FVC (MEF$_{50}$ or Vmax$_{50}$) was observed among non-smoking girls whose mothers smoked. Tager and coworkers (55) suggested that a larger sample might have revealed a similar relationship among boys.

Measures of lung function in Tecumseh children were not entirely independent, because values for children of the same household were correlated. Intraclass correlation coefficients of approximately 0.25 have been observed between siblings, with 0.46 between male siblings and 0.66 between female siblings in Tecumseh (44). When a random sample of one child per household was selected from this population, results were essentially unchanged, demonstrating that a lack of independence would not account for the observed association with passive smoking.

Several investigators have adjusted children's lung function by their parent's lung function (28) or by their parent's body mass (56). It is likely, as suggested by Weiss and associates (57), that this adjustment would mask a true passive smoking effect, should it exist.

Several investigators have attempted to control for potential confounders of the relationship between passive smoking and respiratory outcomes. For example, Fergusson and colleagues (5) demonstrated an increase in bronchitis and/or pneumonia during the first 2 yr of life in children of mothers who smoked after controlling for socioeconomic status, family size, and maternal age. Several investigators have shown that the association of passive smoking with impaired lung function remains significant after controlling for parental education (23, 24), sibship size (21, 23), and the child's own smoking (25). Results from this study indicate that associations of parental smoking with prevalence of respiratory conditions and lung function are independent of parental education and family size.

Cigarette smoking by children may be related to both parental smoking and the respiratory outcomes under study. In this research, significant relationships between measures of passive smoking and respiratory outcomes have been demonstrated among children and adolescents who were presumed to be never smokers. There is a possibility that some of the observed passive smoking effect in children 10 to 15 yr of age might be due to unreported active smoking, and some of the effect in those 16 to 19 yr of age might be due to inaccurate reporting of their smoking habits. In subsequent analyses, subjects who were reexamined 15 yr later and reported cigarette smoking at an age that was younger than their baseline examination in 1962-1965, were also excluded and, in general, results were unchanged. It is unlikely that observed associations between respiratory conditions and parental smoking among the youngest age groups could be explained by active smoking by the children themselves.

Parents who smoke and report respiratory symptoms or illnesses themselves may tend to overreport respiratory conditions in their children; this parental reporting bias has been raised as a possible explanation for passive smoking health effects (6, 7, 16, 17, 27, 57). Schenker and associates (16) suggested that associations between passive smoking and respiratory symptoms and illnesses may be due to shared genetic and/or environmental factors, or to overreporting by symptomatic parents for their children. Weiss and colleagues (58) found an increased risk of atopy in nonsmoking children of smoking mothers that was not explained by maternal reporting bias. When stratification or logistic regression was used in the present research to control for parental reporting bias, trends were occasionally diminished, yet relationships generally remained significant.

It is possible that some of the observed association with passive smoking might be due to gas cooking or heating. The relationship between gas cooking and respiratory conditions (16, 29, 53, 59-61), and associations with lung function have been demonstrated in some studies (23, 29) but not in others (54, 55, 59, 62). Results of a pilot study involving a sample of 213 nonsmoking women from Tecumseh did not show a significant relationship between gas cooking and FEV$_1$ (62). Schenker and associates (16) did not find gas cooking to be an independent risk factor for chronic respiratory symptoms or illnesses.

In general, respiratory conditions were more prevalent and, although not reported here, lung function was lower for male offspring when the only smoker in a household was the mother rather than the father (43). Stronger associations with maternal smoking than with paternal smoking have been observed in a number of studies (5, 15, 16, 21, 23, 53-55, 61, 63, 64). This is consistent with a potentially greater passive exposure of children if their mothers smoke than if their fathers smoke, because of more time spent by offspring in the presence of their mothers during this time period. In this study, associations of passive smoking with respiratory conditions and lung function appeared stronger among younger than among older age groups and among males rather than among females. Higher prevalence rates of respiratory symptoms and illnesses have been observed among younger age groups (2, 5, 21) and among male children (21, 65). Younger age and male sex have been identified as independent risk factors for acute respiratory illnesses and chronic respiratory symptoms (16). Associations between maternal smoking and lung function were strongest among younger male children in one study (64) and among female children in others (21, 24, 26, 54).

The apparent sex difference observed in this research was not explained by a difference in dose or duration of exposure to parental smoking. Confounding by active smoking could account for some of the significant associations observed in males 10 to 15 yr of age if a greater proportion of males than of females were active smokers. However, such confounding would not account for such associations in the younger age groups. As suggested by Taussig and coworkers (66), the sex differential in response to parental smoke exposure may have a physiologic basis. The higher prevalence and incidence of asthma among males, for example, may be consistent with an increased susceptibility of males to sidestream cigarette smoke or other pollutants. Weiss and associates (58) recently demonstrated significantly elevated odds ratios for atopy in males but not in females with a prior history of bronchiolitis or croup.

The magnitude of association between parental smoking and children's lung function appears similar to that found in other studies. Whether a decrement of 144 ml in FEV$_1$ (4.6%) associated with having 2, compared with no, parental smokers will become clinically significant with increasing age remains to be inves-

tigated. Tager and associates (55) recently reported a deficit in expected growth of lung function in children participating in the Six-Cities Study. Additional longitudinal studies should be conducted to further substantiate these long-term adverse effects and to quantitate the magnitude of impact that exposure to parental cigarette smoke may have on respiratory health. More accurate estimates of passive smoking using specifically designed questionnaires and biochemical markers such as cotinine in urine or saliva are needed.

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Study of the Role of Environmental Factors in the Respiratory Health
of Children in Hamilton, Ontario: Epidemiologic Survey Design,
Methods, and Description of Cohort" American Review of Respiratory
Disease 133:   987-993, 1986.

SUMMARY: The relative importance of the effect of outdoor
environmental factors (suspended particulates, sulphur dioxide)
and indoor environmental factors (parental smoking, gas cooking),
on the respiratory health of children is still unclear. To answer
these questions, a 3-yr cohort analytic study has been conducted
in Hamilton, Ontario between 1978 and 1981. The prevalence of
respiratory symptoms and indoor environmental factors was
determined by an interviewer-administered questionnaire. Pulmonary
function measures included both the forced expiratory maneuver and
the single- and multiple-breath nitrogen washouts. Outdoor air
quality was measured by a comprehensive network of suspended
particulate and sulphur dioxide monitors. There were 3,345 children
7 to 10 yr of age studied in the first year, a response rate of
95.4%, 3,727 in the second year, and 3,168 in the third year; 75.6%
of the initial cohort were studied in both Year 2 and Year 3.
Comprehensive quality control in the study included measurement of
the repeatability of both the questionnaire and pulmonary function
data. Repeatability was acceptable except for variables derived
from the single-breath nitrogen washout (correlation between initial
and repeat closing volume vital capacity was 0.14). Cigarette
smoking in Year 3 was reported in 4.8% of the children. The
distribution of other covariables was not uniform, and the
prevalence of parental smoking and gas cooking was greatest in the
industrial area with the highest particulate pollution. Future
analysis of these data will require the effect of these covariables
to be distinguished from that caused by outdoor air pollution.

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A Three-Year Cohort Study of the Role of Environmental Factors in the Respiratory Health of Children in Hamilton, Ontario

Epidemiologic Survey Design, Methods, and Description of Cohort [1-3]

ANTHONY T. KERIGAN, CHARLES H. GOLDSMITH, and L. DAVID PENGELLY

Introduction

The study of environmental factors responsible for respiratory disease in children is important for 2 reasons: (1) the absence of confounding factors, such as personal smoking and occupation, makes the interpretation of any observed association between air quality and respiratory disease more credible; and (2) the growing realization that respiratory illness during childhood may predispose to the development of respiratory morbidity and early mortality from respiratory illness during adult life (1, 2).

This particular usefulness of children has become more important as air quality has improved during the last decade (1970-1979) and levels become closer to the Ontario guidelines. For total suspended particulates (TSP), the Ontario objective (annual geometric mean) is 60 µg/m³. In 1978, the annual TSP in Hamilton was 77 µg/m³. For sulphur dioxide, the objective is 0.02 ppm annual average and the measured level was 0.016 ppm (3).

Studies in several countries from 1967 to 1978 have identified a number of environmental factors that might lead to respiratory disease in children. The initial study of the effect of the particulate/sulphur dioxide (SO₂) complex was conducted by Lunn and coworkers (4) and showed increased prevalence of respiratory symptoms and reduced pulmonary function in areas of poor air quality. Improvement in air quality led to a reduction in these adverse health effects (5). Follow-up studies in several towns in the United Kingdom by Melia and colleagues (6) showed that adverse health effects were now extremely difficult to find with the further improvement in air quality. These studies, however, did not consider the possible role of parental smoking.

As outdoor air quality improved, at-tention changed to indoor air quality, particularly in relation to parental smoking and indoor sources of gaseous pollutants such as gas stoves. The health effects from parental smoking appear to be most marked in the first years of life (7), but studies of this effect on older children have not yielded consistent results, some showing increased prevalence of symptoms (8) but others showing no effect (9, 10). Colley and coworkers (11) suggested that the effect of parental smoking may be due predominantly to the increased prevalence of parental cough. An effect of parental smoking on children's pulmonary function has also been shown (12, 13). The influence of gas cooking was first suggested by Melia and coworkers (14), although the effect seemed to decrease as the children became older. In contrast, Keller and colleagues (15) were not able to find any effect of gas cooking on children's respiratory symptoms. The uncertainty about the role of low levels of TSP and SO₂, and their importance in relation to domestic environmental factors, led us in 1978 to initiate a 3-yr cohort study in Hamilton, Ontario that was designed to answer the following questions. (1) Is there an effect on children's respiratory health of suspended particulates and SO₂ at the present levels? (2) What is the effect of the various factors in the domestic environment when considered in relation to outdoor air quality?

The main study was preceded by a pi-

SUMMARY The relative importance of the effect of outdoor environmental factors (suspended particulates, sulphur dioxide) and indoor environmental factors (parental smoking, gas cooking), on the respiratory health of children is still unclear. To answer these questions, a 3-yr cohort analytic study has been conducted in Hamilton, Ontario between 1978 and 1981. The prevalence of respiratory symptoms and indoor environmental factors was determined by an interviewer-administered questionnaire. Pulmonary function measures included both the forced expiratory maneuver and the single- and multiple-breath nitrogen washouts. Outdoor air quality was measured by a comprehensive network of suspended particulate and sulphur dioxide monitors. There were 3,345 children 7 to 10 yr of age studied in the first year, a response rate of 95.4%, 3,727 in the second year, and 3,168 in the third year; 75.8% of the initial cohort were studied in both Year 2 and Year 3. Comprehensive quality control in the study included measurement of the repeatability of both the questionnaire and pulmonary function data. Repeatability was acceptable except for variables derived from the single-breath nitrogen washout (correlation between initial and repeat closing volume vital capacity was 0.14). Cigarette smoking in Year 3 was reported in 4.8% of the children. The distribution of other covariables was not uniform, and the prevalence of parental smoking and gas cooking was greatest in the industrial area with the highest particulate pollution. Future analysis of these data will require the effect of these covariables to be distinguished from that caused by outdoor air pollution.
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TABLE 1

SUSPENDED PARTICULATE LEVELS BY AREA OF CITY
(JANUARY THROUGH DECEMBER 1980)

	WU	EU	WL	EL	IC
Total suspended particulates, $\mu g/m^3$	44	43	61	58	90
TSP Load < 7.0 μ, %	70.3	86.8	87.9	71.1	82.1
Maximal daily average, $\mu g/m^3$†	140	146	173	149	223
Monitoring sites, n	5	3	9	4	5

Definition of abbreviations: WU = west upper quadrant, EU = east upper
quadrant, EL = east lower quadrant, IC = industrial core.
* Average of annual geometric means of all sites in each area.
† Average of daily maxima of all sites in each area.

lot study (16) which demonstrated that within Hamilton, Ontario, there existed substantial gradients across the city for suspended particulates and SO_2 that would enable us to study children with differing exposures in the same city. This offered major logistical advantages in a design similar to that of Lunn and co-workers (4). During the current study, these gradients for suspended particulates continued to be present. The levels in each area of the city during 1980 are shown in table 1 in terms both of the annual geometric mean and of the daily maximum. The table also shows the proportion of particulate load less than 7.0 μ. Despite the increasing level of particulates towards the industrial core, there is little change in the proportion of particulate matter less than 7.0 μ.

Methods

Design of Study

Hamilton, with a population of approximately 300,000, is a city situated at the western end of Lake Ontario. The dominant geographic feature is an escarpment of approximately 100 m high that runs from east to west, effectively dividing the city into a lower section and a mountain section. The city is industrial, with the heavy industrial core, located in the northeast section of the city, being the dominant producer of particulate and SO_2 emissions, although there is a secondary SO_2 area source in the commercial section located in the western part of the city. Prevailing winds are from the southwest.

Initial air quality monitoring during the pilot study had indicated the presence of substantial gradients for both particulates and SO_2, with the mountain section having lower levels than the lower section of the city. On this basis and on the knowledge of prevailing winds, we divided the city into 4 quadrants (figure 1) for the purpose of selection of the sample to be studied. The sampling frame was all public elementary schools within the city of Hamilton. Sample size considerations dictated that at least 800 children would be required within each quadrant. A difference of 5 to 7% in the mean of a particular pulmonary function variable was felt to be necessary for biologic significance. One of the principal outcomes of interest was the measurement of air flow, especially at low lung volumes. Estimates of the mean and standard deviation of these variables were obtained from our pilot study (16) (FEV_1: mean, 1.79 L; SD, 0.36; MEF_{75}: mean, 1.09 L/s; SD, 0.44). The first criterion employed in sample size determination was that there should be only a 10% chance of missing a biologic difference (Beta error = 0.1). A second criterion was that a difference was considered to exist between the 2 samples if the appropriate statistical test showed that the observed difference had only a 5% chance of occurring in the absence of any real difference (Alpha error = 0.05). Within each of these quadrants, schools were randomly selected until at least 800 children from Grades 2, 3, and 4 during the initial school year had been included. The only children excluded were those older than 10 yr of age by the end of 1978. All children in the required grades from the final school selected in each quadrant were chosen. The children included in the first year of testing made up the initial cohort.

After more detailed air quality monitoring during the first year of the study, it was realized that the area of highest exposure (i.e., TSP annual geometric mean > 60 $\mu g/m^3$) was underrepresented, despite the initial stratification by quadrants in the original design. For this reason, the 3 remaining schools in this area were added, with all children within the required age interval being included.

In addition, in the second year, all children in this same age interval as the initial cohort who moved into a school of study, were included in the study. During the third year, no new children were added.

The questionnaire used in the study was one that we had employed in the pilot study. It was developed from a questionnaire used in a similar study in the European Economic Community. The questionnaire covered several aspects of the child's respiratory history, family smoking and respiratory profile, certain aspects of the child's medical background, and information relating to the quality of the dwelling and socioeconomic circumstances of the family. There were differences between our questionnaire and that developed by the American Thoracic Society (17). In our questionnaire, a distinction was made between morning cough and cough during the day or night, the respondent being asked if the child usually coughed in the morning or during the day or night, respectively. Sputum production was not asked about. The question on wheezing inquired if the chest ever sounded wheezy or whistling. In addition, a question about asthmatic attacks in the previous 12 months was included. Two questions related to acute respiratory illness were included. The first asked about a period of cough and phlegm lasting for 3 wk or more and the second about any chest illness keeping the child home for a week or more. (A detailed questionnaire is available from the writers.) In Year 2, questions about early childhood illnesses were added that were derived from the questionnaire designed by the American Thoracic Society (17). Our questionnaire was administered in the home by a trained interviewer to the mother or female guardian, or in her absence, to the father or male guardian. The questionnaire was administered in each of the 3 yr of the study prior to the performance of pulmonary function testing.

Pulmonary function testing was performed at the child's school. Four types of pulmonary function tests were performed: forced expired maneuvers (FEV_1, FVC, MEF_{50}, MEF_{75}, and MET), spirometry (a slow vital capacity (VC) following quiet breathing) (VC, ERV), single-breath nitrogen washout (CV/VC, N_2 difference) and multiple-breath

Fig. 1. Outline map of Hamilton, Ontario, showing the 4 quadrants chosen in the original design, and the Industrial Core (IC) (WU = west upper; EU = east upper; WL = west lower; EL = east lower).
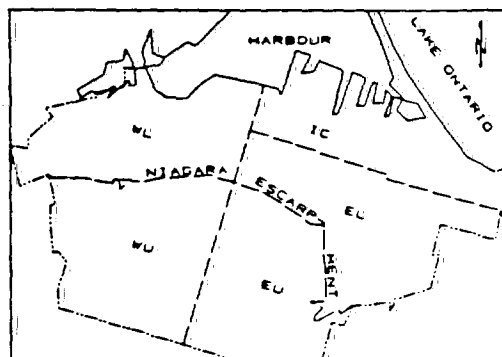
nitrogen washout (FRC). The additional use of the single-breath nitrogen washout was justified by the study of Becklake and coworkers (18), who showed an increase in closing volume in children exposed to a high particulate/SO₂ environment.

Air quality was measured by a comprehensive particulate and SO₂ network. There were 27 monitored sites for TSP using hi-vol samplers, with 9 additional hi-vol samplers with Andersen 4-stage cascade impactors for the measurement of mass median diameter. In addition, there were 16 sites for SO₂ monitored in groups of 8, using Beckman 906A monitors (Beckman Instruments, Fullerton, CA), for 6-wk periods in rotation. These sites were distributed throughout the city. Details of air quality monitoring will be contained in a subsequent report.

Protocol

In the questionnaire survey, interviewers were randomly assigned to eligible children at each school to be visited, thus ensuring that several interviewers would be assigned to each school. In addition, interviewers were rotated to schools in different parts of the city. The parents had been informed in advance by letter to expect a phone call from the interviewer. The letter also described the purpose of the study as being the investigation of the child's respiratory health. No mention was made of air pollution. Each interviewer telephoned the parent or guardian to arrange for an appointment for questionnaire administration. There was provision for 3 call-backs, if no contact was established initially, before no further attempt at interviewing was made. At the time of contact, the interviewer was able to screen out those children who were older than 10 yr of age in the first year of testing. If the parent consented to the interview, they were then visited by the interviewer. The percentage of those eligible, for whom an interview was not obtained, including those with whom no contact could be established, ranged from 4.6% in Year 1 to 3.3% in Year 3 (table 2). No further attempt was made to follow these. Interpreters were used as necessary, but were required for less than 1% of the parents. At the end of the interview, the pulmonary function test was explained to the parent or guardian, and written consent for the test was obtained at that time. The completed questionnaire was then returned for coding, keypunching, and data storage at the Computation Services Unit at the Health Sciences Centre, McMaster University.

Pulmonary function testing was performed, throughout the school year, within 4 wk of the completion of the interview. Two teams of pulmonary function technicians were assigned alternately to a school in the upper and in the lower part of the city. The testing routine was explained initially to all the students at an assembly and explained further to each child at the time of his or her testing. A questionnaire about smoking habits was also administered to the child at the time of testing in the third year of the study. Pulmonary function testing was performed using the Hewlett-Packard 47804A Pulmonary Calculator System (Hewlett-Packard, Waltham, MA). In this system, flow is measured by a pneumotachygraph, and volume is computed internally by integration with time. Calibration of the 2 systems used was performed twice daily with a 2-L syringe. Correction for ambient temperature and pressure was performed internally by the computer system by entering the appropriate values. After measurement of height and weight, the child first performed a multiple-breath nitrogen washout. This was followed by at least 3 forced expired maneuvers. For acceptance, the 2 largest FVC values had to be within 5% of each other. All measurements were taken from the maneuver with the greatest sum of FVC and FEV₁. Spirometry was then performed. If the VC obtained was less than the FVC by more than 10%, the spirometry was repeated until the estimate was within 10%. However, if the VC was greater than the FVC by more than 10%, then the forced expired maneuver was repeated until the FVC estimate was within 10% of VC. Finally, at least 2 single-breath nitrogen washouts were performed in which the expired nitrogen concentration was continuously plotted against VC. The method used was that of Mansell and associates (19), but without the additional dead space. For acceptance of the single-breath nitrogen washout test, the VC had to be within 10% of the largest previous VC from spirometry. If both single-breath maneuvers were acceptable, then the closing volume from the maneuver with the greater VC was taken for analysis. The presence of an upper or lower respiratory infection was noted by the technician at the time of the test. However, the test was always performed, the infection data to be used at the time of analysis to estimate the effect of the infection on pulmonary function. The testing followed the same sequence in Years 2 and 3, except that in Year 3, the single-breath nitrogen washout was omitted because of poor reproducibility (see Discussion). The child was not necessarily tested with the same system nor by the same technician, but comparison of results from the 2 teams was performed at regular intervals to identify any systematic differences.

All measurements of flow and of volume were computed internally, with output being recorded by an on-line printer. Closing volume, however, was computed by inspection of the single-breath nitrogen washout curve, and was taken at that point of inflection of the nitrogen washout curve from a line drawn through phase 3 of the curve (19). These results were then returned for coding, keypunching, and data storage in a manner similar to the questionnaire data.

The quality control of the data gathered was performed in several ways. For both the questionnaire and the pulmonary function coding, a random 5% sample of the data was recoded by a second coder. The reliability of the questionnaire data was estimated by the random selection of 4 interviewers after each pair of schools was completed. For each interviewer, 2 interviews were randomly chosen, and within those interviews, 2 questions were randomly selected. The appropriate respondent was then phoned and the questions were asked again. Apart from estimating the reliability of the answers, this procedure also verified that the original interview had indeed taken place. Interinterviewer variation or bias was estimated by comparing the response rates to certain questions obtained by each interviewer. These data were then examined to see if any differences between interviewers might be greater than that caused by chance alone. When such a difference was found, interviewing technique was reviewed to ensure consistency of technique. In no case was it necessary to change any of the interviewing staff because of poor reliability.

The reliability of the pulmonary function testing was estimated by the retesting of 8 children in each school, 2 children randomly chosen from each age group. All data from pulmonary function testing were passed through a range checking program after data storage, the range being 4 standard deviations centered at the mean, these interval estimates of parameters being derived from the original pilot study. Finally, we were interested in determining any systematic differences between the 2 pulmonary function testing teams. The presence of any differences was estimated by parallel line regression analysis for 4 of the variables measured (FVC, MEF₇₅, MET, and CV/VC). This technique used regression analysis to fit a regression line separately to the data collected by each team; if the linear relationship was the appropriate model, then the hypothesis that the 2 lines were parallel was tested. If this hypothesis was not rejected, then the hypothesis that the intercepts were the same was tested. If the second hypothesis was

TABLE 2

CONSENT AND TESTING RATE FOR SAMPLE

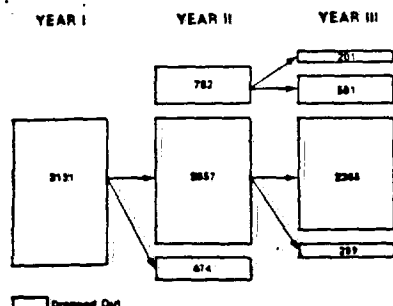|	Year 1	Year 2	Year 3
Eligible for interview	3,505	3,727	3,168
Interviews completed	3,345	3,588	3,065
Interview completion rate, %	95.4	96.3	96.7
Consents given for testing	3,329	3,573	3,055
Consent rate, %	95.0	95.9	96.4
Number tested	3,131	3,439	2,949
Testing completion rate, %	89.3	92.3	93.1

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YEAR I   YEAR II   YEAR III

Fig. 2. Maintenance of cohort size, showing numbers lost by attrition and Industrial Core group added during Year 2.

TABLE 3

CHARACTERISTICS OF SAMPLE TESTED

	Year 1		Year 2		Year 3	
	(n)	(%)	(n)	(%)	(n)	(%)
Male	1,611	51.5	1,789	51.4	1,513	51.3
Female	1,520		1,670		1,436	
Caucasian	2,876	91.9	3,161	91.9	2,723	92.3
Non-Caucasian	255		278		226	
Total	3,131		3,439		2,949	

TABLE 4

PREVALENCE OF DOMESTIC FACTORS BY AREA OF CITY: YEAR 2* *

	WU	EU	WL	EL	IC
Number	829	878	741	863	242
Mother smoke	37.3	42.5	42.2	48.2	60.1
Father smoke	38.3	43.4	43.3	50.2	61.3
Mother cough	15.7	15.0	17.8	17.5	28.5
Father cough	22.1	26.4	26.1	25.6	40.4
Gas cooking	8.3	8.3	29.7	15.6	43.4
Share room with 2 or more	2.3	3.6	7.3	7.0	8.8
Income less than $10k/yr.	15.8	11.3	20.7	15.6	25.9
Less than 2 yr at present address	22.4	19.0	28.2	25.6	34.4

For definition of abbreviations, see table 1.
* Values are percentages. Data missing on 36 subjects.

not rejected then it was concluded that the regression lines for the 2 teams were coincident (20).

A final quality control measure was an examination of the proportion of missing values for each variable for each team, as an indicator of systematic differences between the 2 teams. The analysis and the results of these quality control measures will be described in detail in a separate report. However, the reliability of the questionnaire and pulmonary function data, and the success rates of pulmonary function testing, are described in this report.

Statistical analyses were performed by subprograms in the Statistical Package for the Social Sciences (21). The difference between sample means was tested for significance by subprogram t test for paired samples. Pearson's product-moment correlation coefficient, as a measure of association of 2 independent variables, was computed by subprogram scattergram. Hypothesis tests were all two-tailed.

Results

Characteristics of Cohort

The number who were eligible for testing in each year of the study is shown in table 2. To be eligible, the child could

not have attained his or her eleventh birthday before December 31, 1978. This table also shows the interview completion rate obtained in each year. The rate, which was above 95% for each year, is considered acceptable. In addition, the percentage giving consent for the pulmonary function testing was virtually identical to that giving consent for interview. There was, however, a degree of attrition after consent was given for pulmonary function testing, before the test was performed. The major reason for this was the child having moved from a testing school into a nontesting school during the time between consent and testing. This attrition was less in Years 2 and 3.

An important feature of the study was

the ability to follow the initial cohort into the second and third years of the study. The particular importance of this is the ability to measure changes in pulmonary function variables as the child grows. It is possible that the rate of change of a particular pulmonary function variable might be a more sensitive outcome measure than the use of a single point estimate. The number of children with pulmonary function testing in Year 1 who were tested in Years 2 and 3 (approximately 75% of the original cohort) is shown in figure 2. The figure also shows the number of children added in Year 2 and how many of these were followed into Year 3. The characteristics of the children at the time of pulmonary function

TABLE 5

PREVALENCE OF SMOKING*

	Age (yr)						
	8	9	10	11	12	13	Total
Any history of smoking†							
Yes	0 (0)	57 (11.8)	175 (18.1)	250 (28.3)	186 (37.8)	37 (50.0)	707 (24.3)
No	3	425	791	634	310	37	2,200
Total	3	482	966	884	496	74	2,907
Smoking in last 4 wk‡							
Yes		2 (3.6)	28 (16.4)	41 (17.0)	56 (30.8)	12 (32.4)	139 (20.3)
No		53	143	200	126	25	547
Total		55	171	241	182	37	686

* Values are frequency with percentages in parentheses.
† Missing observations, 158.
‡ Missing observations, 21.

TABLE 6

REPEATABILITY OF RESPIRATORY SYMPTOM QUESTIONS

Question	Raw Agreement	Chance-Corrected Agreement (Kappa)
Cough in morning	0.92	0*
Cough during day or night	0.80	0*
Chest wheezy or whistling	0.80	0.53
Asthma in previous 12 months	0.96	0.76
Cold goes to chest usually	1.0	1.0
Cough and phlegm for 3 wk in previous 12 months	0.95	0*
Absence from school for 1 wk or more in previous 12 months	1.0	1.0

* In each case, one marginal was zero, making Kappa an unreliable estimate of chance-corrected agreement.

testing in each of the 3 yr are shown in table 3. There is a slight excess of males over females in each year, and the predominant Caucasian ethnic characteristic of the sample is to be noted.

Previous studies have shown that certain factors other than outdoor air quality can be related to the incidence or prevalence of childhood respiratory disease (7, 10, 13). The distribution of these factors in each of the 4 original quadrants, and also in the additional group of schools in the industrial core that were added in Year 2, are shown in table 4. In this table, a smoker is one who smokes 1 or more cigarettes or cigars per day. The percentage with cough includes those with a positive answer to either of the questions: "Do you usually cough in the morning?" or "Do you usually cough during the day or night?" To simplify the presentation, only the results from Year 2 are shown. However, those from Years 1 and 3 are similar. The prevalence of these factors varied across the city and was highest in the industrial area, where the level of TSP was also the highest (table 1). A further, potentially confounding covariable was the prevalence of smoking by the children themselves. Because the age interval in the first year was between 7 and 10 yr of age, we did not expect to find many smokers. However, by the third year of the study, it might be expected that some of the older children would have commenced regular smoking. We therefore administered a smoking questionnaire to the children at the time of pulmonary function testing. The number of children in each age group who stated that they had smoked at least 1 cigarette in the last 4 wk is shown in table 5.

Quality Control
The repeatability of the respiratory symptom questions is shown in table 6, which

details the agreement statistics for each of these questions, both in terms of raw agreement and of chance-corrected agreement (Kappa). In certain cases, Kappa was an unreliable estimate of chance-corrected agreement, because one marginal of the 2 × 2 table from which the Kappa was to be computed was zero. Kappa ranged from a substantial level of 0.56 to an excellent level of 1.0. The per-

centage of missing values by team for variables derived from the 4 pulmonary function maneuvers is shown in table 7. The values are shown for Year 1. The commonest reason for a pulmonary function value to be missing was that the child could not meet the required criteria for test acceptance. These results, therefore, give a comparison of ability of the 2 teams in obtaining successful tests for each test in each age group. The repeatabilities of the lung function measurements in Years 1 and 2 of the study are shown in tables 8 and 9. There were small but significant differences for several of the measurements (FVC, MEF$_{50}$, MEF$_{75}$, MET, and VC) in Year 1 and to a larger extent in Year 2. The results for Year 3 are not displayed for sake of brevity, but they showed no significant differences. The product-moment correlation coefficients for certain of these variables are shown in table 10 for Year 1. These range from 0.97 for FVC to 0.14 for CV/VC. The reproducibility of these tests might have been affected by the presence of a respiratory infection during either the ini-

TABLE 7

PERCENTAGE OF MISSING VALUES BY TEAM: YEAR 1

Variable	Team	Age (yr) 6	7	8	9	10	11	Total
FVC	A	0.0	1.0	0.4	2.1	0.3	2.6	1.0
	B	0.0	3.3	1.6	1.3	0.9	3.4	1.8
VC	A	33.3	12.5	5.1	7.5	1.0	0.0	6.4
	B	33.3	11.5	5.4	2.4	1.8	3.4	5.1
FRC	A	16.7	5.8	3.9	4.8	1.0	0.0	3.9
	B	16.7	10.4	5.0	1.5	1.3	3.4	4.4
CV	A	66.7	49.0	28.6	23.8	12.6	5.1	27.7
	B	33.3	37.4	24.2	14.3	9.0	20.7	21.2
N$_2$ difference	A	66.7	49.3	28.8	23.8	12.6	5.1	27.9
	B	33.3	36.5	24.2	14.0	9.0	20.7	21.3
Children tested, n	A	6	304	532	480	266	39	1,647
	B	6	270	501	456	223	29	1,485

Definition of abbreviations: CV = closing volume; N$_2$ difference = increase in expired nitrogen concentration during phase III of single-breath nitrogen washout.

TABLE 8

REPEATABILITY OF LUNG FUNCTION MEASUREMENTS: YEAR 1

Variable	n	Initial Mean	SD	Repeat Mean	SD	t Value	p Value (2-tailed)
FVC	216	2.04	0.41	2.07	0.41	-3.96	< 0.001
FEV$_1$	216	1.67	0.31	1.66	0.31	1.33	0.190
MEF$_{50}$	215	2.33	0.62	2.14	0.59	3.57	< 0.001
MEF$_{75}$	211	0.99	0.36	0.94	0.32	3.45	0.001
MET	215	0.57	0.17	0.59	0.18	-3.13	0.002
VC	220	2.05	0.41	2.06	0.40	-3.30	0.001
FRC	210	1.19	0.31	1.19	0.29	0.13	0.895
CV/VC	186	0.134	0.09	0.12	0.078	1.42	0.158
N$_2$ diff	180	1.04	0.86	1.03	0.52	0.13	0.900

Definition of abbreviations: MET = midexpiratory time in seconds. For other definitions, see table 7.

TABLE 9
REPEATABILITY OF LUNG FUNCTION MEASUREMENTS: YEAR 2

Variable	n	Initial		Repeat		t Value	p Value (2-tailed)
		Mean	SD	Mean	SD		
FVC	256	2.37	0.47	2.35	0.51	2.24	0.026
FEV$_1$	256	1.91	0.36	1.88	0.39	2.66	0.008
MEF$_{50}$	254	2.46	0.63	2.39	0.66	2.64	0.009
MEF$_{75}$	254	1.05	0.34	1.03	0.35	1.49	0.138
MET	256	0.59	0.16	0.60	0.19	-1.79	0.75
VC	255	2.39	0.47	2.36	0.49	2.37	0.019
FRC	253	1.32	0.33	1.31	0.34	0.37	0.713
CV/VC	226	0.12	0.08	0.12	0.09	-0.13	0.897
N$_2$diff	226	0.88	0.50	0.85	0.44	1.35	0.178

For definition of abbreviations, see tables 7 and 8

tial or the repeat test. The repeatabilities of the lung function measurements were therefore reanalyzed, omitting from the analysis any test during which the presence of an upper or lower respiratory infection had been recorded. The results from this analysis are shown in table 11. Comparison with table 9 does not indicate that the reproducibility of the test was improved by the exclusion of current respiratory infections. In addition, for no variable was the product-moment correlation coefficient changed by the exclusion of respiratory infections.

Discussion

This report outlines the background to the study that has been undertaken, the design of this study, and the methods that were used, and it describes the sample that was studied, both in terms of its characteristics and also in terms of important covariables. The design of the study was innovative in selecting schools within each of 4 quadrants of the city in expectation that these areas would show different levels of air quality. However, the area of the city with TSP levels greater than 60 μg/m³ annual geometric mean was underrepresented when the air quality results from the first year were analyzed. This required the addition of 3 schools in the industrial core in the second year to achieve a gradient of air quality that one might expect to show an effect on the child's respiratory health. Financial constraints often dictate that air quality monitoring is done at the same time as the measurements of respiratory disease outcomes in children or in adults. However, without detailed prior information about the distribution of air quality gradients, modification of the design may be required during the course of the study, with the increased difficulty this might give in the analysis of the results. Random selection of schools within each quadrant was performed for this health study in the first year but not with the additional schools in the second year, because all the schools in the industrial core (that is, the area of highest particulate levels) were chosen for inclusion in the study.

The cooperation obtained from the Board of Education for the City of Hamilton and the parents of the children was excellent. We feel that the response rate in excess of 95% obtained in each year enables us to extrapolate any conclusions from the sample chosen to the total population of children at risk.

It was not surprising to find that the

distribution of covariables, which might influence the child's respiratory health, was not uniform across the city. In the examination of the relationship between levels of air pollutants and respiratory health, it is very important that any confounding effect of covariables be distinguished from the effect of air pollution itself. We have shown that the industrial area, which has the highest level of TSP, has also the highest prevalence of domestic smoking, parental respiratory symptoms, and gas cooking. (22).

A further important consideration in the study of the effect of air quality on respiratory health is the previous mobility of the sample being studied. As table 4 shows, the proportion of children who had lived at their present address for less than 2 yr varied from 34.4% in the industrial core to 19.0% on the eastern part of the mountain. This difference would also have to be taken into account in any analysis of these results.

Cigarette smoking by the children themselves also becomes important in this particular age group as it can lead to respiratory disease. Tager and coworkers (23) showed that children's smoking habits must be taken into account when looking at any putative effect of parental smoking. Direct validation of the estimates of smoking obtained from our smoking questionnaire was not performed. However, the percentage of children admitting to smoking in the previous 4 wk does increase in the expected direction with increasing age. In addition, these data are comparable to those obtained by Brown and colleagues (24) in their survey of smoking habits in Canadian school children. We are therefore confident that these results do reflect the smoking habits of the children. However, the rate of 4.8% who had smoked in the previous 4 wk is unlikely to affect the interpretation of the results.

TABLE 10
PRODUCT-MOMENT CORRELATION COEFFICIENT OF INITIAL AND REPEAT ESTIMATES OF PULMONARY FUNCTION VARIABLES

	Year 1	Year 2
FVC	0.97	0.86
FEV$_1$	0.94	0.83
MEF$_{50}$	0.78	0.74
MET	0.72	0.81
RV	0.40	0.43
CV/VC	0.14	0.03

TABLE 11
REPEATABILITY OF LUNG FUNCTION MEASUREMENTS RESPIRATORY INFECTIONS EXCLUDED: YEAR 1

Variable	n	Initial		Repeat		t Value	p Value (2-tailed)
		Mean	SD	Mean	SD		
FVC	159	2.02	0.41	2.04	0.41	-3.47	<0.001
FEV$_1$	159	1.66	0.30	1.64	0.30	0.97	0.37
MEF$_{50}$	158	2.26	0.61	2.15	0.58	3.26	0.001
MEF$_{75}$	158	1.00	0.34	0.94	0.32	2.99	0.003
MET	158	0.56	0.17	0.58	0.16	-2.93	0.004
VC	162	2.03	0.40	2.05	0.40	-2.55	0.012
FRC	157	1.17	0.32	1.17	0.29	-0.31	0.76
CV/VC	123	0.14	0.08	0.13	0.08	1.33	0.19
N$_2$diff	120	1.01	0.59	1.06	0.50	-0.13	0.90

For definition of abbreviations, see tables 7 and 8

The results of a number of quality control procedures were part of the study. The repeatability of the respiratory symptom questions was estimated only when those particular questions were asked from the randomly chosen questionnaires. We thought it important to compute chance-corrected agreement (Kappa), because the raw agreement, when the prevalence of a particular symptom is low, may give a false impression of good agreement, when in fact most of the agreement is due to chance alone. For 3 cases, Kappa could not be computed. On the other hand, by the criterion of Landis and Koch (25), agreement was substantial or better for the questions on asthma, colds to chest, and absence from school for more than 1 wk with a chest illness. It was only slightly less than substantial for the question on wheezing or whistling in the chest.

The ability of young children to perform pulmonary function maneuvers is shown in table 7. The forced expired maneuver was the one most successfully performed. In the older age groups, slow spirometry and the multiple-breath nitrogen washout were equally well performed. In contrast, the single-breath nitrogen washout had a failure rate in excess of 20%. This lack of success for this particular test did not improve in Year 2 and it has been our experience that the single-breath nitrogen washout test is a difficult maneuver to employ in large scale epidemiologic monitoring in children.

In tables 8 and 9, it can be seen that in Years 1 and 2 there were small but significant differences between the initial and repeat estimates of a number of the pulmonary function variables that were not due to the presence of a respiratory infection. The differences were not found to be significant, however, in Year 3. No significant differences were found between the initial and repeat estimates for the variables derived from the multiple- and single-breath nitrogen washout maneuvers. However, for these variables, the coefficient of variation was much greater than for the variables derived from the forced expired maneuver, and therefore the analysis was less powerful in being able to demonstrate a difference if one really existed. An additional measure of association, the correlation coefficient, was high for the variables (FEV, and FVC) derived from the forced expired maneuver, but was much less for those variables derived from the single-breath nitrogen washout. This low correlation reduces considerably the usefulness of

the single-breath nitrogen washout test because the amount of random variation may well obscure any true difference between samples.

In conclusion, we have described the design and execution of a study of the effects of environmental factors on the respiratory health of children within a single city. The random selection and high response rate have ensured that the sample is characteristic of the population of interest in the city. The accurate estimation of pollution exposure has required a more comprehensive network of air quality monitors than would normally be employed in a single city. The non-uniform distribution within the city of covariables, such as parental smoking and cough, has implications for the detection of the effects of suspended particulates and SO_2, especially when those effects are likely to be small at current levels of these pollutants. If present, these effects are only likely to be detected with samples as large as the one that we have studied.

Pulmonary function testing, even in the youngest of children, had a high rate of success with the exception of the single-breath nitrogen washout. We were disappointed with the lower rate of success of this test, its greater degree of variability, and its lack of reproducibility. For these reasons, it was omitted from the Year 3 testing; we feel that its place in large scale epidemiologic testing has not been justified.

Acknowledgment

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Value
tailed)

0.001
0.37
0.001
0.003
0.004
0.012
0.76
0.19
0.90

28

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Salzman, M.B., Biller, H.F., Schechter, C.B. "Passive Smoking and Croup" <u>Arch Otolaryngol Head Neck Surg</u> 113:866-868, 1987.

ABSTRACT: The relationship between croup and the presence of household cigarette consumption was assessed in a matched-pair case control study. Fifty subjects with a primary hospital discharge diagnosis of croup were paired with children with a primary hospital discharge diagnosis of abdominal hernia. The results yielded an estimated relative risk of 0.82. The power of this study to detect a relative risk of 2.0 was 38%. This study fails to show a relationship between passive smoking and croup in early childhood.

Passive Smoking and Croup

Mark B. Salzman, MD; Hugh F. Biller, MD; Clyde B. Schechter, MD

• The relationship between croup and the presence of household cigarette consumption was assessed in a matched-pair case control study. Fifty subjects with a primary hospital discharge diagnosis of croup were paired with children with a primary hospital discharge diagnosis of abdominal hernia. The results yielded an estimated relative risk of 0.82. The power of this study to detect a relative risk of 2.0 was 38%. This study fails to show a relationship between passive smoking and croup in early childhood.

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The deleterious effects of cigarette smoking on health are well established. The health effects of passive smoking remain a more controversial topic. *Passive smoking* is the involuntary exposure of tobacco combustion products to nonsmokers from the smoking of others. The small child is particularly vulnerable to passive smoking exposure from household members. There are many studies in the literature linking parental cigarette smoking to respiratory tract infections in children. Studies about the effects of passive cigarette smoking in children have shown the following: (1) increased frequency of lower respiratory tract infections, especially bronchitis and pneumonia, in infants younger than 1 year[1,3]; (2) increased respiratory syncytial virus infection[4,5]; (3) exacerbation and increased risk of asthma and the atopic state[6,7]; and (4) reduced lung function in older children detected through spirometry.[8,11]

The relationship between parental smoking and croup has not received much attention in the literature. Lebowitz and Burrows[12] reported that there was no significant difference in the prevalence rate of croup (as well as bronchiolitis and pneumonia) between children of smokers and nonsmokers; however, no data were presented. Gardner et al[13] also found no association between croup and parental smoking. Their data only mention the total number of episodes of croup in a group of children with parents who smoke compared with the total number of episodes of croup in a group of children with parents who do not smoke. The data do not reveal what percentage of each group of children suffered from croup.

There have been studies linking maternal smoking to the atopic state in children[6] and exacerbating asthma in children.[7] Because spasmodic croup, a common form, may be associated with an allergic state,[14,15] it may also be influenced by passive smoking. The risk for viral and spasmodic croup may increase with parental smoking. Respiratory syncytial virus infection was linked to parental smoking in several studies.[16] Respiratory syncytial virus accounts for up to 12% of viral croup cases in some investigations.[16]

Although there were several studies[12,13] that found no relationship between parental smoking and croup, these studies either presented no data or questionable data. The following study is done to demonstrate whether a relationship between passive smoking and croup exists.

SUBJECTS AND METHODS

The population under study consisted of children younger than 5 years who were discharged from the Mount Sinai Hospital in New York City between 1979 and 1985. The majority of the patients (58% of the study population) are black and Hispanic and from lower socioeconomic classes.

A matched-pair case control study was done. Telephone numbers were obtained from the medical charts of patients in the target population who had primary hospital discharge diagnosis of croup or abdominal hernia. Data were then collected through telephone interviews. Data from croup subjects were collected first and then appropriate hernia subjects were chosen to obtain matched pairs. Criteria for match-pair selection were as follows: (1) same ethnic group (white, black, or Hispanic), (2) hospital admission dates within one year of each other, and (3) age (either younger or older than 1 year). Ethnic group was controlled because of the different prevalence rates of smoking among these different groups (whites less than blacks and Hispanics). All 50 pairs fell into one of these three different groups. Hospital admission dates were controlled since the overall prevalence of smoking in the population decreased between 1979 and 1985. One croup subject could not be matched with this criterion and was subse-

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quently matched with a hernia subject admitted 18 months later rather than within 12 months. Age was also used as a criterion because many studies[13] have only shown a relationship between passive smoking and respiratory illnesses in children younger than 1 year.

The mother of the subject was sought for the telephone interview but if not available, information was taken from a household member. The questions asked were as follows: (1) Who took care of the child in the months preceding the hospitalization? (2) Who smoked cigarettes during this time? (3) In which ethnic group do the parents consider the child?

Only cigarette smoking was included. Questions about pipe, cigar, and recreational smoking were not asked, although these may be important contributing factors.

There were 169 children younger than 5 years with a primary hospital discharge diagnosis of croup between 1979 and June 1985. All of these charts were requested and 147 of these were received from the Medical Records Department. One hundred twenty-four of these charts contained telephone numbers; 65 of these numbers were either wrong or disconnected. No answer was obtained with eight after calling between five and ten times at different times of different days. Fifty-one households were reached by telephone. One refused to participate, leaving a sample size of 50 subjects.

The target population consisted of 370 children with a primary hospital discharge diagnosis of abdominal hernia. Our request for all of these charts produced 312. Two hundred sixty-five had telephone numbers. Date of hospital admission and age were the two criteria used in determining which hernia subject would be used when more than one appropriate case was available. The closest matched subjects for these two criteria were called first. One hundred twelve hernia subjects needed to be called to obtain the 50 matched subjects. There were 61 wrong or disconnected numbers and one no answer.

RESULTS

Each subject was first classified as either living in a home with at least one cigarette smoker or living with no cigarette smokers. The 50 matched pairs fall into the categories as shown below:

Hernia	Croup	
	Smokers	No Smokers
Smokers	15	11
No smokers	9	15

There are actually more pairs with the croup subjects in the homes with no smokers and hernia subjects in the homes with smokers than the converse. The estimated odds ratio is less than one (9/11 or 0.82), which is not significant ($x^2 = 0.80$ and must be greater than 3.841 when $\alpha = .05$). Since there are only 20 discordant pairs among the 50 pairs shown, the power of this study to detect a twofold increased risk is only 38%. A 2.0 relative risk is approximately the increased risk found in most studies[13] linking parental cigarette smoking to bronchitis and pneumonia in children, although the most recent Surgeon General's report states that children of smokers had a 20% to 80% greater risk of respiratory problems than other children.[17] Therefore, the power of this study may even be less than 38%.

The literature[3] has shown the effect of maternal smoking as more important than parental smoking in increasing the risk for respiratory illnesses in children. This requires investigation of maternal smoking as an isolated factor. These results are shown in the following:

Hernia	Croup	
	Maternal Smokers	Maternal Nonsmokers
Maternal smokers	5	12
Maternal nonsmokers	8	25

Once again we see more pairs with maternal smokers for patients with hernia and maternal nonsmokers for patients with croup than the converse. The estimated odds ratio equals 0.67.

Many studies[13] show only children younger than 1 year at an increased risk for developing a respiratory illness from passive smoking. Therefore, children younger than 1 year are categorized separately. The results are shown below:

Hernia	Croup	
	Smokers	No Smokers
Smokers	5	5
No smokers	2	7

Nineteen pairs contained children younger than 1 year. We again have an estimated odds ratio of less than one (0.40).

The following shows the results when only maternal smoking is examined with children younger than 1 year. The estimated odds ratio is exactly 1.

Hernia	Croup	
	Maternal Smokers	Maternal Nonsmokers
Maternal smokers	2	3
Maternal nonsmokers	3	11

Each interviewee was also asked who took care of the child during the day in the months preceding the hospitalization. This was asked because this person probably had the greatest contact with the child and this person was sometimes not the mother. The following shows the results when the smoking history of this caretaker is examined separately. The estimated odds ratio is less than 1 (0.90).

Hernia	Croup	
	Smokers	Nonsmokers
Smokers	3	10
Nonsmokers	9	28

The following shows the results when the smoking history of the caretakers and only children younger than 1 year are examined.

Hernia	Croup	
	Smokers	Nonsmokers
Smokers	1	3
Nonsmokers	4	11

The estimated odds ratio is 4/3 or 1.33. The difference is not significant.

COMMENT

Data do not support the hypothesis that passive cigarette smoking increases the risk for croup in young children. The power of this study does indicate that the study population may not have been large enough. When we examine the 50 pairs of subjects, there were only 20 discordant pairs in the analysis involving the presence of household smokers. This does not furnish sufficient statistical power for this study. Most studies[13] finding an association between parental smoking and bronchitis and pneumonia only found about a twofold increased risk. If the risk for croup is increased by parental smoking, then the increased risk is

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probably about twofold as it is for bronchitis and pneumonia. We need 55 discordant pairs to achieve a statistical power of 80%. The statistical power is only 38% with 20 discordant pairs.

Another limitation of this study is that the target population only includes children who were hospital-ized for croup. Because croup is predominantly an outpatient disease, the population under study may not be a representative sample of children afflicted with croup.

The literature[1-17] has shown that parental smoking can adversely affect the health of children. Although this study does not support the hypothesis that passive smoking increases the risk for croup, the power of this study is too small to draw conclusions. A larger study is warranted.

This study was submitted as partial fulfill-ment of the clerkship requirement in Community Medicine while Dr Salzman was a third-year medical student at the Mount Sinai School of Medicine, New York.

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Editorial Footnote

This interesting epidemiologic pilot study contains important new scientific information and provides an opportunity to review and relearn some valuable features and some limitations regarding survey research of this type.

One of the disappointing aspects of the report is the absence of data regarding the amount of smoking activity to which the child was exposed. Other reports dealing with the direct effect of smoking on individuals have been careful to include quantitative information describing the amount of smoking that has occurred. If one is investigating a particular cause-and-effect relationship, the dosage (number of cigarettes smoked) of the supposed causative factor is a central issue to validity and reliability as one deals with conclusions regarding the effects.

Even though this particular report contributes no valid scientific information concerning the risk of passive smoking, the authors have introduced a research methodology that, under appropriate circumstances, has the capability of detecting such effects. The authors certainly did the right thing, but, unfortunately, the limits of the study did not result in a definitive outcome from the sample that was used. The ultimate purpose of this study was to demonstrate whether a relationship exists between passive smoking and croup. The results permit no accurate determination

of the strength of this relationship. The Surgeon General's office now reports a definite association between passive smoking and respiratory disease in infants. If my understanding of the Surgeon General's report is correct, then I suggest that the authors are accurate when they propose that a broader study should definitely be designed and funded. Having said all of this about the shortcomings of the study, I hasten to congratulate the authors for having undertaken such a difficult task and for having accomplished as much as possible within the limitations of their resources.

BYRON J. BAILEY, MD
Chief Editor

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Fleming, D.W., Cochi, S.L., Hightower, A.W., Broome, C.V. "Childhood Upper Respiratory Tract Infections: To What Degree Is Incidence Affected by Day-Care Attendance?" Pediatrics 79(1):55-60, 1987.

ABSTRACT: Risk factors for acute upper respiratory tract disease in childhood were evaluated in a population-based sample of the Atlanta metropolitan area. Mothers from 449 households containing 575 children less than 5 years of age were selected by random-digit dialing and questioned about upper respiratory tract infection and ear infection occurring in their children during the preceding 2 weeks. Household demographic and socioeconomic characteristics, maternal smoking history and child day-care attendance and breast-feeding information were also obtained. For children less than 5 years of age, the reported incidence of upper respiratory tract infection was 24%, and of ear infection, 6%. Controlling for the other variables measured, day-care attendance was associated with a significantly increased risk of both illnesses. For upper respiratory tract infection, increased risk was present for all children attending daycare (P = .02, odds ratio = 1.6), whereas for ear infection, risk could be demonstrated only for full-time attendees (P = .005, odds ratio = 3.8). Maternal smoking was a second independent risk factor for a child's having upper respiratory tract infection (odds ratio = 1.7, P = .01). Thirty-one percent of all upper respiratory tract infection among day-care attendees and 66% of all ear infections among full-time day-care attendees were attributable to day-care attendance. Given the proportion of children in day-care, 9% to 14% of the total burden of upper respiratory tract disease in this population was day care related. As use of child day-care facilities has increased, this specific exposure has become a major factor contributing to transmission of acute upper respiratory tract disease in childhood.

Childhood Upper Respiratory Tract Infections: To What Degree Is Incidence Affected by Day-Care Attendance?

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ABSTRACT. Risk factors for acute upper respiratory tract disease in childhood were evaluated in a population-based sample of the Atlanta metropolitan area. Mothers from 449 households containing 575 children less than 5 years of age were selected by random-digit dialing and questioned about upper respiratory tract infection and ear infection occurring in their children during the preceding 2 weeks. Household demographic and socioeconomic characteristics, maternal smoking history and child day-care attendance and breast-feeding information were also obtained. For children less than 5 years of age, the reported incidence of upper respiratory tract infection was 24%, and of ear infection, 6%. Controlling for the other variables measured, day-care attendance was associated with a significantly increased risk of both illnesses. For upper respiratory tract infection, increased risk was present for all children attending day care ($P = .02$, odds ratio = 1.6), whereas for ear infection, risk could be demonstrated only for full-time attendees ($P = .005$, odds ratio = 3.8). Maternal smoking was a second independent risk factor for a child's having upper respiratory tract infection (odds ratio = 1.7, $P = .01$). Thirty-one percent of all upper respiratory tract infection among day-care attendees and 66% of all ear infections among full-time day-care attendees were attributable to day-care attendance. Given the proportion of children in day care, 9% to 14% of the total burden of upper respiratory tract disease in this population was day care related. As use of child day-care facilities has increased, this specific exposure has become a major factor contributing to transmission of acute upper respiratory tract disease in childhood. *Pediatrics* 1987;79:55-60; *upper respiratory tract infection, day-care attendance.*

Infections of the upper respiratory system are the most common illnesses affecting children less than 5 years of age in the developed world. Although

these illnesses, including acute upper respiratory tract infection and otitis media, may occasionally progress to more severe disease, most often they are self-limited. Despite their relatively benign nature, however, upper respiratory tract infectious illnesses are important causes of childhood morbidity, and their treatment consumes a substantial portion of available health care resources.[1]

During the past decade, it has been demonstrated that risk of a number of childhood infections, including hepatitis,[2] diarrheal diseases,[3] and invasive *Haemophilus influenzae*,[4] is increased by day-care attendance. During this same time, the number of children younger than 5 years of age in the United States who are enrolled in day care has undergone a dramatic increase.[5] Although several studies have suggested that the risk of upper respiratory tract disease may be increased for some day-care attendees,[6-8] the importance of this association has not been well defined.

In this study, we examined risk factors for acquisition of infections of the upper respiratory system in children less than 5 years of age and specifically evaluated the role played by day-care attendance. Using population-based data, we determined the amount of illness attributable to this increasingly common childhood exposure.

METHODS

A cross section of all households containing children less than 5 years of age in Atlanta was surveyed by telephone from mid-July through mid-September 1984.

Sampling Procedure

Telephone numbers consisting of prefixes serving the study area and four randomly selected final

digits were generated by computer. Every possible telephone number in the seven counties composing the metropolitan area (population 1.9 million) had an equal likelihood of being selected and called; no call-clustering techniques were used. Each number selected was called at least twice during business hours and at least six times during evenings and weekends before being discarded. Only households with children less than 5 years of age were enrolled.

Questionnaire Administration

Using a standardized questionnaire, trained interviewers obtained informed consent and then collected information from the guardian of the children in the household, preferably the mother. Data obtained included household demographic and socioeconomic characteristics, current maternal smoking history, and current breast-feeding and day-care attendance information for all children less than 5 years of age. All children within a given household were enrolled to ensure that our sample accurately represented all children in the study area with respect to household size and other related characteristics. A 15% sample of completed questionnaires was validated with a follow-up telephone call; no child's illness or day-care status was reclassified as a result of these calls.

Definitions

History of recent acute respiratory infection (cough, cold, or ear infection) was obtained directly from the child's guardian.[6,7,9] Because independent physician confirmation of illness was not required, we have used the term "ear infection" rather than otitis media to denote parental reported cases of infections of the ear. Criteria including antibiotic administration and physician visit were used if respondents needed clarification. We did not attempt to identify specific etiologic agents. Incidence of disease rather than duration of symptoms was assessed. To limit interviewer and respondent bias, illness history was elicited before parents were asked about day-care attendance. Children were considered case children if they had been ill with upper respiratory tract infection or ear infection at any time during the 2 weeks before the interview was conducted. Day care was defined as regular (>4 h/wk) supervised care of at least two unrelated children. Each child's day-care status was determined individually, based on enrollment at the time of interview. Part-time enrollment was defined as five to 39 hours' attendance per week and full-time as 40 or more hours per week.

Analysis

Two analyses of risk factors were undertaken, one for children reported to have upper respiratory tract infection and the other for children reported to have ear infection. An automatic interaction detection program was used to assist in selection of variables for inclusion in an unconditional logistic regression model. Only associations that were biologically plausible were considered. We did not attempt to analyze or control for transmission of illness within households because we could not distinguish between primary and secondary cases. The number of children younger than 5 years in the household, a variable included in the model, may serve as a surrogate for intrafamilial spread. Final models were obtained by first putting all candidate variables into the model and then eliminating any variable that was not significant and whose elimination did not alter the odds ratio estimates of significant variables by more than 15%. Etiologic fractions among exposed groups (EFe) were calculated by the formula: $EFe = $ (probability of disease in exposed − probability of disease in unexposed)/(probability of disease in exposed) and were standardized for the entire population by weighting the values from individual strata according to the percentage of the population represented by that strata. The disease probabilities used were those determined by the regression model.

RESULTS

A total of 3,952 households in the study area were surveyed. Of these, 3,387 contained no children younger than 5 years, 78 were unwilling to answer whether children were present and 487 contained at least one young child. Of these latter households, complete interviews were obtained for 449 (92%). Twenty-six percent of households (118) contained more than one child, and information regarding illness was collected for 575 children.

Upper Respiratory Tract Infection

Twenty-four percent of the children surveyed (139/575) were reported to have had an upper respiratory tract infection during the 2 weeks before the interview. The incidence of reported illness was divided equally by sex with 24% of both boys (75/307) and girls (64/268) affected. Race did not appear to be a significant risk factor; illness was reported for 23% of white children (96/421), 27% of black children (40/146), and 40% of children of other races (4/10). The frequency of upper respiratory tract infection did vary somewhat with age; incidence in children younger than 36 months was 27% (91/338), and in children 36 months or older, 20% (47/232).

On univariate analysis, children who attended

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day-care facilities appeared to be more likely than children who did not attend to have had symptoms of an upper respiratory tract infection during the 2 weeks preceding the interview (32% [55/175] of attendees v 21% [84/400] of nonattendees; $P = .01$, x^2). A significant difference in risk between part-time and full-time attendance could not be demonstrated, although there was a suggestive trend in children younger than 36 months (42% [23/55] incidence in full-time attendees v 28% [11/39] in part-time attendees, $P = .2$, Fisher exact test). The type of day-care facility, ie, residential v nonresidential, and the length of time the child had been attending were not statistically associated with the likelihood of upper respiratory tract infection.

The association of day-care attendance with upper respiratory tract infection was further evaluated by logistic regression in a model that contained other variables considered to be possible risk factors for disease. These variables included family income, crowding (dichotomized at less than v equal to or more than one person per room), and number of children less than 5 years of age, maternal smoking, and child's race and age (dichotomized at 36 months). Current breast-feeding was included as a possible protective factor in children less than 6 months of age.

In this model, children who attended day care were significantly more likely than children who did not attend to have had a parent-reported upper respiratory tract infection during the 2 weeks before interview (odds ratio = 1.6, $P = .02$, Fig 1). In addition to day-care attendance, a second factor, maternal smoking, was also associated with increased risk of upper respiratory tract infection (odds ratio = 1.7, $P = .01$). The effects of day-care attendance and maternal smoking were independent of one another. Child's age, although itself not

a risk factor (odds ratio = 1.2, $P = .4$), did significantly modify the effect of a third variable, household crowding. Living in crowded conditions was significantly associated with upper respiratory tract infection in children younger than 36 months (odds ratio = 2.4, $P = .02$) but not in children 36 months or older (odds ratio = 0.6, $P = .4$). No statistically significant association with risk of upper respiratory tract infection was seen for family income, number of children less than 5 years, and child's race, and no protective benefit of breast-feeding could be demonstrated (Table 1).

Clustering of illnesses within households did not seem to significantly affect the association of upper respiratory tract infection with day-care attendance. This relationship in households with only one child less than 5 years of age was similar to that in households with two ill children (odds ratio = 1.73 v 1.72), and the prevalence of day-care attendance in ill children from households containing no other children less than 5 years was similar to that observed in children from households with another ill sibling (41% [35/85] v 40% [12/30]).

Ear Infection

Six percent (34/575) of children less than 5 years of age were reported to have had an ear infection during the 2 weeks before the interview. Ear infection was reported more often for boys than girls (7.2% v 4.5%), but this difference was not statistically significant. Black children and white children were affected equally (6.1%); none of the ten children of other races were reported ill. Compared with upper respiratory tract infection, the incidence of ear infection was more influenced by age. Incidence was 8.6% (29/337) in children 0 to 35 months of age and 2.1% (5/233) in children 3 or 4 years of age. Children with ear infection were significantly more likely than children without ear infection to have had upper respiratory tract infection symptoms during the preceding 2 weeks (65% [22/34]) v 22% [116/535]; odds ratio = 6, $P < .001$, Fisher exact test).

Univariate analysis suggested that, as with upper respiratory tract infection, children attending day
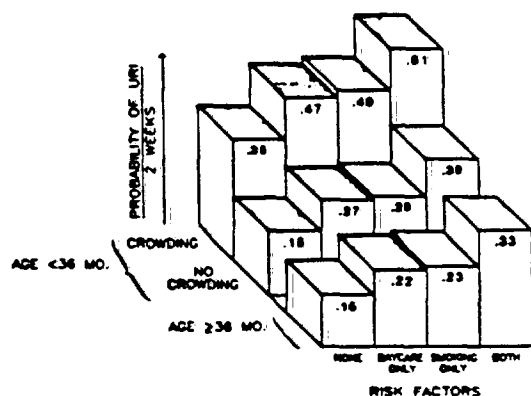

Fig 1. Probability of upper respiratory tract infection according to age, crowding, maternal smoking, and day-care status.

TABLE 1. Variables Not Included in Final Upper Respiratory Tract Infection Model

Variable	Odds Ratio (Point Estimate)	P Value
No. of children <5 yr	0.7	.17
Race	1.1	.76
Breast-feeding	1.0	.98
Income ($)		
0-19,999	1.0	
10-34,999	1.5	.14
≥35,000	1.0	.91

care were at increased risk for development of ear infection. For ear infection, however, only children who attended a day-care facility 40 or more hours per week could be shown to be at increased risk. This association with full-time attendance was present when either all children or only children younger than 36 months were evaluated (Table 2). Although the number of children with ear infection who attended day-care full time was relatively small, the type of day-care facility, ie, residential υ nonresidential, and the length of time the child had been attending did not appear to be associated with increased risk of disease.

The association between full-time day-care attendance and ear infection was evaluated in a logistic regression model containing the same variables that were used for the upper respiratory tract infection analysis. Concomitant upper respiratory tract infection was not considered as a separate risk factor because this illness may, in many instances, represent an intermediate step between exposure to a risk factor and ear infection.[8,10] Clustering of ear infections within a household occurred only once and, thus, was not a factor in analysis. In the ear infection model, full-time day-care attendance was strongly associated with increased risk of ear infection (odds ratio = 3.2, P = .005). Age was a second important predictor of disease, with children younger than 36 months at higher risk than children 36 months of age or older (odds ratio = 3.3, P = .02). Among young children, as with upper respiratory tract infection, crowding was an important factor predicting disease (odds ratio = 3.4, P = .01); in the older age group, data were insufficient to assess the effect of this variable (Fig 2). For ear infection, family income, number of children less than 5 years of age, maternal smoking, and child's race and breast-feeding status were not significantly associated with risk (Table 3). Two factors, maternal smoking and part-time day-care attendance, which were associated with the risk of upper respiratory tract infection, were not associated with the risk of ear infection. This finding may be due to the smaller numbers of children with ear infections and consequent lack of statistical power or
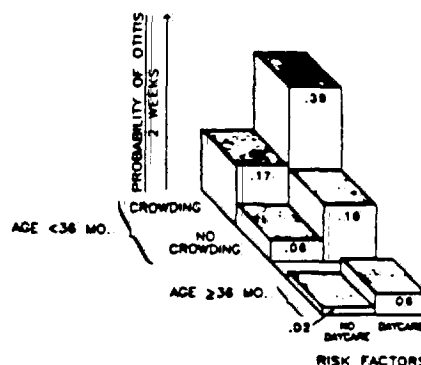

Fig 2. Probability of ear infection according to age, crowding, and day-care status.

TABLE 3. Variables Not Included in Final Ear Infection Model

Variable	Odds Ratio (Point Estimate)	P Value
No. of children <5 yr	0.7	.43
Maternal smoking	1.1	.82
Race	1.0	.93
Breast-feeding	1.9	.32
Income ($)		
0–19,999	1.0	
20–34,999	0.9	.87
≥35,000	0.8	.73

alternatively to actual differences in risk factors for these two syndromes.

Attributable Risk

Perhaps the most meaningful measure of the amount of upper respiratory tract disease associated with day-care attendance is the etiologic fraction among the exposed children or $EFe_{(day-care)}$, which can be interpreted as the proportion of respiratory illness among children who attend day care that is directly related ("attributable") to this exposure.

In this study, the $EFe_{(day-care)}$ for upper respiratory tract infection, adjusted for the other variables shown to be associated with upper respiratory tract infection, was 31%. Thus, approximately one third of upper respiratory tract infections in children who attend day care may be attributable to this specific exposure. The $EFe_{(day-care)}$ for upper respiratory tract infections varied slightly by age and was 30% for children younger than 36 months and 33% for children 36 months of age or older.

For ear infections, the $EFe_{(full-time\ day-care)}$ was 66%, standardized for the other variables shown to be associated with ear infection, and thus approximately two thirds of ear infection contracted by full-time day-care attendees may be directly re-

TABLE 2. Incidence of Ear Infection by Day-Care Attendance Status for All Children and Children 0 to 35 Months of Age

Day-Care Attendance Status	Incidence of Ear Infection (%)	
	All Children	0–35 Mo
Nonattendees	4.8 (19/395)	7.0 (17/244)
Part-time attendees	4.1 (3/73)	5.3 (2/38)
Full-time attendees	11.7 (12/102)	18.2 (10/55)
Status not available	(0/5)	(0/1)
Total	5.9 (34/575)	8.7 (29/338)

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TABLE 4. Etiologic Fraction Among Exposed Groups (EFe$_{day\text{-}care}$) and Population Attributable Risk of Upper Respiratory Tract Infection and Ear Infection Associated with Day-Care Attendance

Child's Infection and Age (Mo)	EFe$_{(day\text{-}care)}$	Children Attending Day-Care (%)	Population Attributable Risk (%)
Upper respiratory tract			
0–35	.30	29	9
≥36	.33	34	11
Ear infection			
0–35	.64	16	10
≥36	.68	20	14

lated to that specific exposure. The age-specific EFe$_{(full\text{-}time\ day\text{-}care)}$ for ear infection was 64% for children 0 to 35 months of age, those at highest risk, and 68% for children 3 and 4 years of age.

The amount of upper respiratory tract disease in all young children that is directly related to day-care attendance (the etiologic fraction among the population, also called the population attributable risk) depends not only on the proportion of illness related to attendance but also on the proportion of children who attend. This latter figure is likely to depend on a variety of factors including geographic region, season of the year, and age of the children involved. In Atlanta, during the summer of 1984, the population attributable risk for day-care attendance varied between 9% and 11% for upper respiratory tract infection and between 10% and 14% for ear infection, depending on child's age (Table 4).

DISCUSSION

Although more than 11 million children in the United States attend some form of day care,[11] estimates of risk have not been available for many of the illnesses to which these children are exposed, and the need for population-based studies has become increasingly apparent.[11,12] In particular, although the association between day-care attendance and infections of the upper respiratory system was suggested more than 35 years ago,[13] the contribution of day-care exposure to overall risk for these diseases has not been defined.

This study was designed to quantify the relation between day-care attendance and risk of childhood upper respiratory tract infections. Controlling for the effect of other risk factors, children in this cohort who were enrolled in day care were substantially more likely to have both upper respiratory tract infection and ear infection. Because these children were randomly selected from the general population, we could calculate that approximately

one third of upper respiratory tract infections among day-care attendees and two thirds of ear infections among full-time day-care attendees were directly related to attendance. Because data regarding the proportion of children in the population attending day-care facilities were also available, we were able to estimate that 9% to 14% of all upper respiratory tract infections and ear infections in children less than 5 years of age may occur as a result of day-care attendance, a figure generalizable to other areas to the extent that day-care attendance patterns in Atlanta are similar to attendance patterns elsewhere. These estimates provide a useful assessment of the influence of day-care attendance on the overall risk of upper respiratory tract infection in young children. Respiratory illness results in an estimated 17.4 million physician visits a year in the United States[1] and for otitis media alone, an estimated annual expenditure of more than $2 billion.[14]

These percentages should be interpreted with appropriate caution. Having a child in day care may alter the likelihood that parents will notice and report illness in their children. This study determined a point estimate of risk based on parental reporting of illness during a 2-week period and, as such, should be viewed as only a first step in quantifying the effect of day-care attendance on the incidence of childhood upper respiratory tract infections. Nevertheless, the case definition based on parental reporting can be partially validated by the results of the analysis. If parents were reporting respiratory infections when no illness had occurred, one would not expect to find significant associations with crowding or maternal smoking. The substantial portion of upper respiratory tract infection linked to day-care attendance in this study suggests that it would be useful to determine whether specific etiologic agents may be particularly associated with this risk.

Additional studies that assess risk over season should be undertaken. For example, the risk of upper respiratory tract infection associated with day-care attendance calculated by this study may be a minimum estimate; day-care attendance may be more strongly linked with disease during the winter respiratory illness season when the likelihood of the introduction of upper respiratory tract infection into a day-care facility may be greater. Alternatively, a greater background incidence of viral infection during the winter might reduce the added risk associated with day-care attendance.

Several aspects of analysis other than the relation between upper respiratory tract illness and day-care attendance deserve comment. The similarity of the risk factor models for upper respiratory tract

infection and ear infection demonstrates the close association between these two illnesses and reaffirms the likely role of upper respiratory tract infections in the pathogenesis of ear infection.[8,10] The data regarding maternal smoking underscore the link between passive exposure to smoke and development of upper respiratory tract infection in children.[15,16] In this study, the proportion of upper respiratory tract infections in children of smoking mothers attributable to this exposure (34%) and the total population attributable risk (10%) were comparable to those calculated for day-care attendance.

As risk factors, however, there is a major difference between maternal smoking and day-care attendance. Whereas maternal smoking is totally preventable, day-care attendance is not. This difference highlights an increasingly obvious dilemma: child day care provides an irreplaceable service; yet, by its nature, it also results in enhanced transmission of infectious illnesses. The most practical approach to this problem—reduction of risk among those children who attend—rests on the assumption that differences in day-care facilities and children's exposures within those facilities may affect degree of risk. For diarrheal disease, this assumption seems warranted; risk has been shown to be influenced by a variety of specific day-care characteristics.[3] Whether the same is true for respiratory disease remains an open question. Identification of specific factors that are associated with increased risk of upper respiratory tract disease within day-care facilities should be a primary goal of future study.

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Cogswell, J.J., Mitchell, E.B., Alexander, J. "Parental smoking, breast feeding and respiratory infection in development of allergic diseases" Archives of Disease in Childhood 62: 338-344, 1987.

SUMMARY: Environmental factors were examined as determinant of clinical disease in a five year prospective study of 73 children born to atopic parents. Clinical follow up for evidence of eczema and wheezing was combined with regular skin testing, immunoglobulin assay, and respiratory viral culture where appropriate.

Thirty six children developed eczema, which was often associated with a positive result of a skin test to ingestants in the first year and inhalants by the fifth year. Thirty two children developed one or more episodes of wheeze. Fifteen children wheezed once only, and not all of these developed atopy.

No pattern of respiratory infection in early life was characteristic of children with recurrent wheeze. There was a significant difference in parental smoking habits between children with and without episodes of wheeze at the fifth birthday. No protective effect of breast feeding could be shown.

The development of allergic disease in susceptible children is influenced by many environmental factors. Advice to families about reduction of environmental allergens continues to pose problems, but parents should be advised to avoid smoking in the child's presence.

Parental smoking, breast feeding, and respiratory infection in development of allergic diseases

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SUMMARY Environmental factors were examined as determinants of clinical disease in a five year prospective study of 73 children born to atopic parents. Clinical follow up for evidence of eczema and wheezing was combined with regular skin testing, immunoglobulin assay, and respiratory viral culture where appropriate.

Thirty six children developed eczema, which was often associated with a positive result of a skin test to ingestants in the first year and inhalants by the fifth year. Thirty two children developed one or more episodes of wheeze. Fifteen children wheezed once only, and not all of these developed atopy.

No pattern of respiratory infection in early life was characteristic of children with recurrent wheeze. There was a significant difference in parental smoking habits between children with and without episodes of wheeze at the fifth birthday. No protective effect of breast feeding could be shown.

The development of allergic disease in susceptible children is influenced by many environmental factors. Advice to families about reduction of environmental allergens continues to pose problems, but parents should be advised to avoid smoking in the child's presence.

The relation between the atopic state and the clinical expression of diseases such as bronchial asthma or atopic dermatitis remains unclear. Most young children with these disorders are atopic and exposure to allergen can, in sensitive individuals, induce bronchospasm and eczematous skin changes. Not all atopic subjects, however, develop disease. The possibility that additional influences are required for expression of disease to occur has received much attention. There have been reports on the role of diverse environmental factors in atopic subjects, including season of birth,[1] respiratory infections.[2] and state of breast feeding.[3–8] In this five year prospective study we have followed a cohort of children (n=97) at risk of allergic disease, seeking the development of eczema, recurrent wheezing, and seasonal rhinitis. We have attempted to examine how environmental factors interact on the atopic constitution and produce symptoms of disease. The incidence of early respiratory infections and the development of specific antibody to common allergens in these children has previously been reported.[9,10]

Patients and methods

Study design. One hundred babies were selected for study before birth on the grounds that one parent gave a history of hay fever or asthma. This selection was designed to provide a cohort of children of whom about half would be expected to develop evidence of atopy, those without atopy acting as controls. In this study atopy was defined as the presence of eczema and/or one or more positive results of a cutaneous prick test to common allergens. Written consent from pregnant mothers was obtained after full explanation that the baby would be subjected to venepunctures and the passage of a soft nasal catheter during the course of the study. All the babies were born in the maternity department of a district general hospital. The mean birth weight on leaving hospital was 3280 g.

At one year there were 92 families on follow up. Most of the study families continued to live in the area served by the hospital, and 73 remained on follow up on the child's fifth birthday (Table 1). Parents were asked to keep a diary of their feeding

Table 1 *Reasons for the 27 withdrawals from the study*

Reason	No
Moved away	12
Lost to follow up	10
Parents decided not to continue	4
Other reason	1
Total	27

methods and smoking habits. The date of the first cow's milk feed was recorded. but this information was not available to the paediatrician (JJC) who examined the babies. The social class classification was recorded (Registrar General's Classification, 1971).

Clinical assessment. All babies were examined at birth, at 3, 6, and 12 months, and annually thereafter. At each hospital visit a clinical history was taken and added to by a daily record of respiratory symptoms and skin problems kept by the parents. Clinical examination of the skin and the respiratory tract was carried out at each visit. In addition, parents were asked to notify the hospital whenever respiratory symptoms developed; a clinical examination was then made, usually at home. A diagnosis of eczema was made when the skin of the face or flexures showed roughening, redness, or intense pruritus that persisted for four weeks or more. Transient spots or cradle cap were not regarded as eczema. The presence of eczema and wheezing was confirmed in all cases by the paediatrician (JJC) or general practitioner. Hay fever was regarded as present if nasal discharge occurred in at least two spring/summer seasons. In this report children are regarded as atopic if they developed eczema or had at least one positive result of a cutaneous prick test during the study.

Laboratory investigation. At each hospital visit immediate skin testing for hypersensitivity was carried out by prick testing with six common allergens—namely, *Dermatophagoides pteronyssimus* (house dust mite), mixed grass pollen, cat fur, dog dander, hen's egg, and cow's milk (Bencard Ltd). A control solution and a 1/1000 histamine solution were also used. The diameter of the wheal was recorded at 15 minutes; a positive reaction was recorded when a wheal was 3 mm greater than that of the negative control. All subjects showed reactivity to the histamine solution.

At each visit venepuncture was performed and the serum assayed for immunoglobulin concentrations, including total serum IgE.[11]

Direct viral culture was attempted whenever respiratory symptoms were notified. Nasopharyngeal secretions were taken from the symptomatic baby in the home and transported at 0°C to the laboratory. The methods of tissue culture have been described elsewhere.[9]

Saliva samples were collected from all children at 3 years. These samples were assayed for IgA, using a double antibody radioimmune assay.[12] This assay is specific for alpha determinants on IgA, is not inhibited by secretory piece, and is not influenced by the molecular weight of the IgA.

Statistical analysis was undertaken using analysis of variance, t test, and χ^2 test. As a result of skewness in the distribution of the IgE results, data were logarithmically transformed ($\log(1+x)$) before significance tests were performed.

Results

Clinical disease. Of the 73 children who remained on follow up for five years, 36 developed eczema. In 34
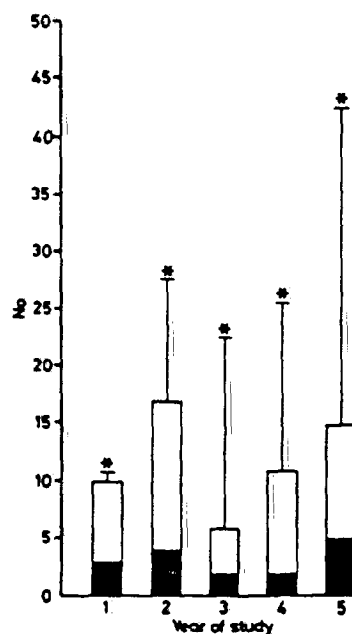

Fig. 1 *Incidence of wheezing by year of study. Total bars (white + black) show number of children who experienced episodes of wheeze in each year; black bars show number of these children who had eczema in each year. Asterisk denotes total number of episodes of wheeze in each year.*

(94%) of these the skin rash became apparent within the first two years of life. In most (n=31) the skin rash persisted for less than one year and did not present an important clinical problem. In five subjects persistent skin inflammation, requiring appropriate topical treatment, was present, but even in these children there was a tendency to improve with age.

Thirty two children (44%) had one or more episodes of wheezing. Most children (69%) had their first episode within the first two years of life. Fifteen children had a episode of wheeze on a single occasion only. Four of the 15 children who wheezed only once showed no evidence of atopy during the five year follow up. As the remainder (n=17) went on to develop recurrent attacks of wheezing the actual number of episodes of wheeze each year increased with age (Fig. 1). Eleven had four or more attacks in the five years and all of these received medical treatment, including admission to hospital in two cases. Fifteen of the 17 children with recurrent wheeze either developed eczema or had multiple positive results of cutaneous prick tests during the study.

Skin tests and clinical disease. The skin test reactiv-ity to the six common allergens is shown in Figure 2. Responses to egg and milk were most prevalent in years one and two, after which they decreased, whereas those to the major inhalant allergens house dust mite and grass pollens were more prevalent in the later years of the study. Of the 36 children with a diagnosis of eczema, 21 were atopic on the basis of results of the skin test. Eleven of these showed egg sensitivity in the first year compared with only three of the 37 children without eczema (p<0.05). During the first year ingested allergens accounted for 86% of positive reactions in children with eczema (Table 2). By contrast, at year five, inhalant allergens accounted for 26 of 27 positive reactions in children with eczema.

Children with recurrent wheezing showed an increasing number of positive reactions to inhalant allergens as age increased, with 16 of 18 being classified as atopic on this basis at the end of the study. Of the 32 children who wheezed, 22 had at least one positive result of a prick test. No character-istic pattern of skin test responses occurred in children with wheeze to distinguish them from the atopic subjects who did not wheeze. Six of the eight patients with hay fever developed a positive skin reaction to mixed grass pollens within five years.
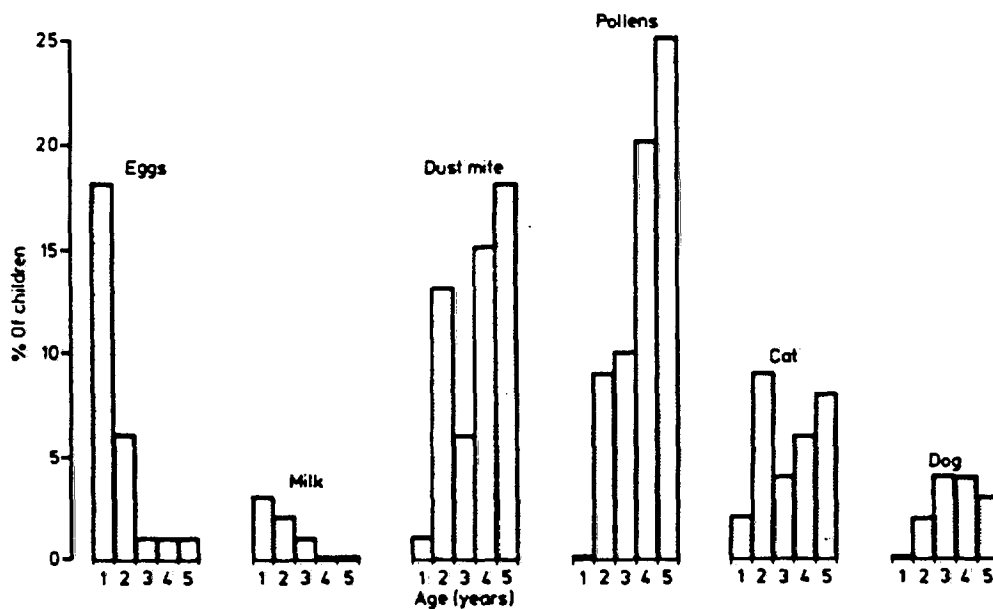

Fig. 2   *Percentage of children with positive results to skin tests for the six common allergens.*

Table 2 *Positive reactions to skin tests at 1, 2, 3, and 5 years in 36 children who developed eczema*

Age (years)	Antigen					
	Egg	Dust mite	Pollens	Cat	Dog	Milk
1	6	—	—	1	—	3
2	4	7	5	4	1	2
3	1	4	4	3	2	1
5	1	10	11	3	2	—

Immunoglobulin concentrations and clinical disease. Immunoglobulin E concentrations were significantly raised in both patients with eczema (Fig. 3) and those with recurrent wheezing (Fig. 4) when compared with those children who did not have these diseases at all ages after 3 months ($p<0.05$). Children who wheezed only once had IgE concentrations that were not significantly different from those of children who did not wheeze at all ($p>0.05$).

No differences in serum IgA concentrations were apparent at any age between 3 and 60 months between children with and without eczema. The salivary IgA values in 3 year old subjects were not significantly different in those with and without eczema, all being within the normal adult range.[6] There was no significant difference in serum IgA concentrations between those who did and did not have episodes of wheeze ($p<0.05$).

Parental smoking. At the children's first birthday the number of those who had developed or were to develop wheezing was equally distributed between parents who did or did not smoke at that time. By 5 years, however, 62% of parents who smoked had children who had experienced episodes of wheeze compared with 37% in families where the parents did not smoke. The difference was significant ($p<.05$) (Fig. 5).

When total serum IgE concentrations of children were compared between the families where the parents smoked and those where the parents did not smoke no significant difference could be found at any age ($p>0.05$).

Respiratory infections. Successful isolations of virus became less common as the children grew up, probably due to sampling difficulties. In all subjects throughout the study respiratory viruses (rhinovirus, respiratory syncytial virus, and para-influenza virus) were isolated from children with both coryzal and wheezy syndromes. The 15 children who wheezed only once often had associated coryzal symptoms. In this group five positive respiratory viral isolates were made (three respiratory syncytial virus, two para-influenza virus).

Respiratory infections occurred more often in the atopic children (mean 20·7 over five years) than in the non-atopic children (mean 15·6), but this difference did not reach significance. There was a similar
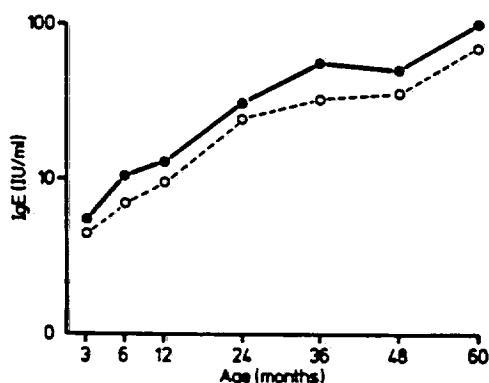

Fig. 3 *IgE concentration in children according to whether they developed eczema or not.* ●——● = *Those with eczema (n = 36); ○- - -○ = those without eczema (n = 37).*
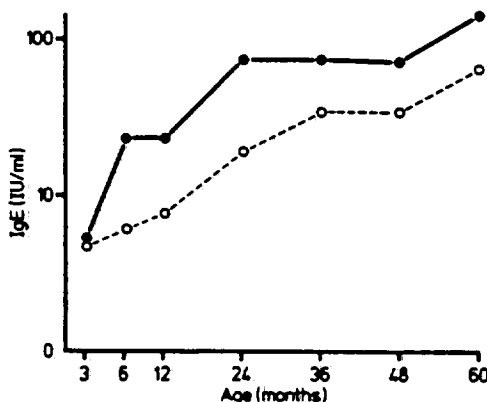
Fig. 4 *IgE concentration in children according to whether they had episodes of wheeze or not.* ●——● = *Those with recurrent wheeze; ○- - -○ = those without wheeze.*
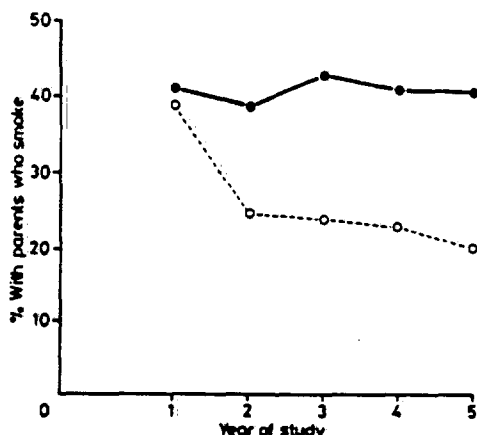
Fig. 5 Parental smoking habits and wheezing in total study population. ●——●=Children with wheeze (n=32); ○- - -○=children without wheeze (n=41).

pattern of respiratory virus infections in the atopic children during the first year of life compared with those who did not develop wheezing (Table 3).

Breast feeding. The duration of breast feeding was taken as the time from birth to the introduction of the first cow's milk or cow's milk formula feed.

In all, 55% of children received no cow's milk during the first four weeks of life and 12% were totally breast fed for over three months.

There was no evidence of any relation between the duration of breast feeding and the incidence of eczema or positive skin tests (p>0·05) (Table 4).

No protective effect of breast feeding against asthma could be shown.

Atopic children and environmental factors. Forty eight children were identified as atopic. Twenty two developed episodes of wheeze and 26 did not. As the genetic predisposition to atopy was similar the two subgroups were compared for environmental influences.

No significant differences between the groups could be shown for social class, season of birth, or duration of breast feeding. The atopic children who

had episodes of wheeze did not have significantly more respiratory infections, and the virus isolates in the first year were similar in both groups (Table 3).

There were significantly more parents who smoked cigarettes among the families of atopic children who had episodes of wheeze at 5 years of age than in the families of children who did not have episodes of wheeze (p<0·05) (Fig. 6).

Discussion

The prediction that roughly half of these children

Table 4 Duration of breast feeding according to atopic state

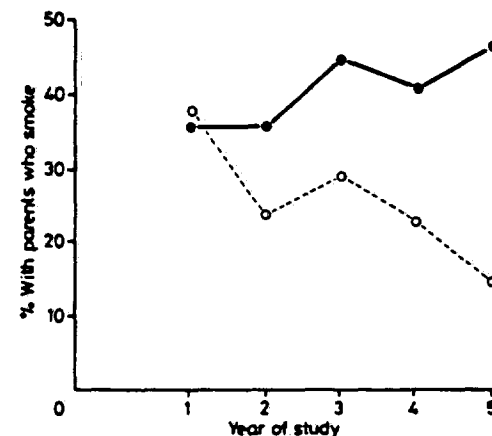| Atopic state	Duration of breast feeding (weeks)			
	>4	5–13	14+	Total
None	14	10	1	25
Skin test positive only	4	7	1	12
Eczema only	7	6	2	15
Skin test positive and eczema	8	8	5	21
Total	33	31	9	73

Fig. 6 Parental smoking habits and wheezing in the atopic study population. ●——●=Atopic children with wheeze (n=22); ○- - -○=atopic children without wheeze (n=26).

Table 3 Virus isolations in 48 symptomatic children with atopy in first year of life

Wheezy children			Non-wheezy children		
Isolates		No	Isolates		No
Rhinovirus	Type H	2	Rhinovirus	Type M	2
Para-influenza	3	3	Para-influenza	3	3
Influenza	A	1			
Respiratory syncytial virus		1	Respiratory syncytial virus		1

would develop allergic disease proved to be correct.[13] The predominant clinical problem was eczema, although most of the children were affected in the first two years only. Over 40% of the children had one or more positive results to a skin test, a prevalence in agreement with a previous report on similar children.[14] Most of the children with eczema were atopic, supporting an association between disease expression and the genetic predisposition to develop IgE antibody responses. The most commonly identified skin sensitivity in the first year was to egg protein. The skin reaction was often transient, disappearing in the second year at a time when the prevalence of eczema was also decreasing. These results suggest a role for food specific immune responses in the pathogenesis of infantile eczema, as has been suggested by others. Skin reactivity to inhalant allergens represented the predominant sensitivity in older children with eczema, although it developed later than that to foods. The role of inhalant allergens in the pathogenesis of eczema has received somewhat less attention. It has been shown that the raised IgE concentrations of children and adults with this disorder includes inhalant allergen specific IgE antibody.[15] The presence of this antibody is not explained by concomitant respiratory allergic disease. Furthermore, the application of such allergens to the skin has been shown to induce eczematous lesions in sensitive individuals.[16] Both ingested and inhaled allergens are probably of clinical importance in subjects with eczema, though their predominant effects may be at different stages of development.

In this study the children who wheezed on four or more occasions all showed evidence of atopy. The predominant sensitivity was to the major inhaled allergens. The results suggest that this preschool chest disorder is indistinguishable from asthma. Not all atopic children develop asthma, suggesting that atopy alone does not give rise to symptoms. Children who wheeze once only in the early months of life do not necessarily go on to show evidence of atopy, and their IgE concentrations are the same as those children who have no episodes of wheeze. Such episodes are usually associated with coryzal symptoms, suggesting that a single episode of wheeze can result directly from respiratory infection of this age.

As in our earlier report,[3] we were again unable to confirm the observation that children with atopic symptoms had a transient deficiency of IgA concentration at 3 months.[17] Differences in study design, clinical definitions, and duration of follow up may account for the conflicting results. We were unable to show that either month of birth or social class influenced the onset of asthma, but it would require

much longer epidemiological studies[18][19] to detect this influence.

This study confirms other observations that respiratory viruses can be isolated from young children during episodes of wheeze.[20][21] The same viruses were isolated, however, from children with coryzal symptoms in both atopic and non-atopic children. These findings suggest that viral infection against an atopic background does not adequately explain all symptoms. No virus, or group of viruses, could be identified as more asthmagenic than others. Due to sampling difficulties in older children, this study was unable to confirm the role of viral infections in the development of recurrent wheezing.

It is known from epidemiological studies that exposure to cigarette smoke doubles the risk to the infant of an attack of pneumonia or bronchitis.[22] Our study suggests that this risk is not confined to infancy and parental smoking habits but may have an even stronger influence on the pathogenesis of wheezing in the 5 year old child. The mechanism of this effect is unclear. In adults smoking may result in an increase in bronchial hyperactivity,[23] this change being only weakly dependent on the atopic state of the patient. Immunological variables can be altered in smokers, including a rise in IgE concentrations. In this study the children of parents who smoked did not show raised IgE concentrations, perhaps suggesting a different mechanism. We have reported elsewhere that the immune response to house dust mite was increased in those children exposed to higher concentrations of its major allergen, antigen p1.[10] These differences include prevalence of skin test reactivity and radioallergosorbent test specific for *D pteronyssimus*. It has been shown previously that avoidance of house dust mite both in children and young adults can result in a reduction of bronchial hyperactivity.[24][25] It is quite clear that recurrent wheezing develops in these subjects who are genetically predisposed to develop an atopic state. It is possible that cofactors, or environmental influences, such as parental smoking, house dust mite antigen, and respiratory tract infections, either by a direct effect on airway reactivity or by altering the nature of the immune response to particular allergens, are required to allow disease expression. The possibility of a synergistic effect between these factors must also be borne in mind.

Breast feeding failed to show any protective effect against the development of allergic disease, including eczema. Whether breast feeding affords protection against atopic disease remains controversial.[3-6] Random controlled clinical trials have given conflicting results. As it is difficult to control how mothers feed their babies many studies have been of an observational design. Our study can be criticised

on these grounds. Bias may have arisen if those infants most at risk opted into the breast feeding group. As the risk was equal among all babies this seems to be unlikely. Moreover, the number of breast fed babies in the trial was similar to local practice at the time. Observer bias was minimised by the clinician being unaware of the feeding history at the time of the clinical assessment. Our conclusions are similar to other recent reports.[7 8]

The finding that egg sensitivity, as shown by immediate skin test reactivity, can occur in wholly breast fed babies suggests that maternal diet may be of relevance. Food allergies in fully breast fed infants have been described.[26] It has been shown in experimental rats that repeated low dose exposure through breast milk increases the likelihood of developing an IgE antibody response to a food protein.[27] The increased incidence of skin tests positive to egg, in breast fed babies compared with bottle fed babies, during the past six months suggests that similar events may occur in man. While breast feeding should continue to be recommended by paediatricians as the best available feed for most babies, we do not believe that it can be promoted as a preventative measure in those infants at risk of developing allergic disease. Studies on the role of maternal exclusion dieting while breast feeding are indicated.

In conclusion, the development of asthma and eczema in susceptible children seems to be influenced by a wide variety of environmental factors. The issue of dietary exposure is as yet unresolved. Exposure to inhalant allergens such as the house dust mite can be reduced, although it is not clear what level of reduction is required to alter the natural history of the disease.[28] The simplest advice that we can give the parents of atopic children is to stop smoking in the child's presence.

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Taylor, B., Wadsworth, J. "Maternal smoking during pregnancy and lower respiratory tract illness in early life" <u>Archives of Disease in Childhood</u> 62: 786-791, 1987.

SUMMARY: In a national study of 12743 children maternal, but not paternal, smoking was confirmed as having a significant influence on the reported incidence of bronchitis and admission to hospital for lower respiratory tract illness during the first five years of life. Reported rates of admissions to hospital for lower respiratory tract diseases were found to be as high in children born to mothers who stopped smoking during pregnancy as in those whose mothers smoked continuously both during and after pregnancy. Rates of admissions to hospital for lower respiratory tract diseases in children whose mothers started smoking only postnatally were no higher than in those whose mothers remained non-smokers. Postnatal smoking seemed to exert a significant influence on the reported incidence of bronchitis, but less than smoking during pregnancy.

These findings suggest that maternal smoking influences the incidence of respiratory illnesses in children mainly through a congenital effect, and only to a lesser extent through passive exposure after birth.

Maternal smoking during pregnancy and lower respiratory tract illness in early life

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SUMMARY In a national study of 12 743 children maternal, but not paternal, smoking was confirmed as having a significant influence on the reported incidence of bronchitis and admission to hospital for lower respiratory tract illness during the first five years of life. Reported rates of admissions to hospital for lower respiratory tract diseases were found to be as high in children born to mothers who stopped smoking during pregnancy as in those whose mothers smoked continuously both during and after pregnancy. Rates of admissions to hospital for lower respiratory tract diseases in children whose mothers started smoking only postnatally were no higher than in those whose mothers remained non-smokers. Postnatal smoking seemed to exert a significant influence on the reported incidence of bronchitis, but less than smoking during pregnancy.

These findings suggest that maternal smoking influences the incidence of respiratory illnesses in children mainly through a congenital effect, and only to a lesser extent through passive exposure after birth.

Parental smoking has been incriminated as having a major adverse influence on the respiratory health of young children.[1-4] Fergusson *et al* found that only maternal, and not paternal, smoking was influential.[5 6] They suggested that fathers who smoked have less contact than mothers with young children, and so there is less irritation of the child's lower respiratory tract from passively inhaled smoke of paternal origin. There are other possible explanations. Maternal cigarette smoking during pregnancy is a health hazard to unborn children, affecting birth weight and predisposing to abortion;[7-9] some studies have suggested that there is an increase in congenital abnormalities in children born to mothers who smoke.[10-13]

Smoking by the mother during pregnancy may cause a congenital predisposition in the child to subsequent respiratory illnesses; we investigated this possibility using data from a national birth cohort study.

Subjects and methods

CHES (the Child Health and Education Study) is a continuing survey of children studied neonatally in the British Births Survey.[14 15] The cohort originally comprised all children born in the United Kingdom, including Northern Ireland, from 5 to 11 April 1970 inclusive. In 1975, 12 743 children of the 16 015 born in that week and living in England, Scotland, and Wales were traced (79.6%). Health visitors interviewed the mothers at home and gathered over 500 items of information about social background, family, and health, including whether the child had had any episodes of bronchitis during the first five years, and whether the child had been admitted to hospital with a lower respiratory tract illness (wheezing, bronchitis, bronchiolitis, or pneumonia) and at what age.

At the interview in 1970 information had been gathered about the mother's smoking habit in pregnancy, the average number of cigarettes smoked each day, the time of giving up smoking if the mother was a previous smoker (recorded as months before delivery), as well as the child's birth weight and any neonatal problems. At the five year interview information was collected about the reported number of cigarettes, if any, smoked by each parent and the duration of regular smoking by each parent since the child's birth.

To allow for factors that could influence both smoking and respiratory illnesses the following

information collected at the five year interview was included in multivariate analyses: sibling ranking at five years, the health visitor's assessment of the home equipment (luxurious, high standard or average, low, very low standard), whether the child had been breast fed, the number of times the family had moved house in the child's first five years, and the social index[16]—that is a composite assessment of socioeconomic state including domestic crowding, parental education, tenure of accommodation, type of neighbourhood, and paternal occupation.

The social data obtained in 1970 were less extensive than those obtained in 1975. The following factors were assessed: social class and mother's age, marital state, and length of full time education. Preliminary analysis included two way tabulations and χ^2 calculations; for multivariate analyses logistic analysis of multiway contingency tables[17] using the generalised linear interactive modelling statistical package GLIM[18] was used to allow assessment of individual factors after simultaneous adjustment for all other factors in the model.

Where there were missing data (never more than 5% and usually less than 2%) as complete a set as possible was used in the analysis. Thus the denominators used to obtain percentages in the tables exclude missing values.

Results

Initial cross tabulation showed that rates of lower respiratory tract illness in the children increased the more the mother smoked. This was so for smoking both during pregnancy and also subsequently (Figure). These dose response relations remained highly significant ($p < 0.001$) and were only slightly attenuated when allowance was made in multivariate analyses for the possible effects of birth weight, social index, home assessment, household moves, number of siblings, and breast feeding. Tables 1 and 2 show the relations between respiratory illness in the children and parental smoking habits and confirms the findings of Fergusson *et al.*[5,6] Data collected at five years were used
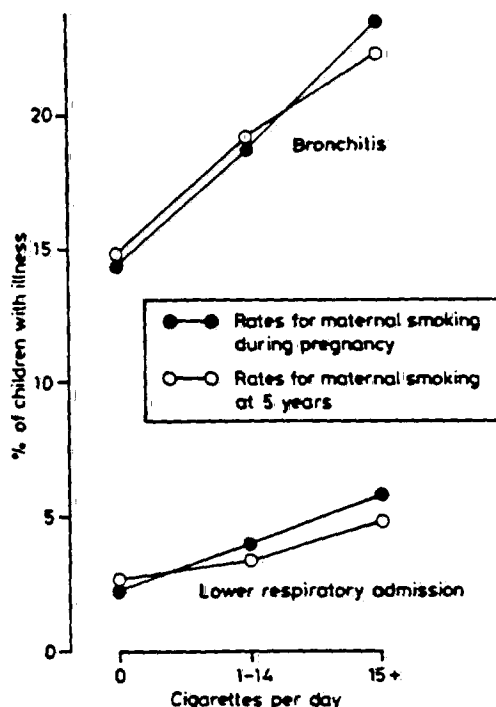

Figure   *Comparative effect of increasing levels of maternal smoking during and after pregnancy on risk of bronchitis and admissions for lower respiratory tract disease in children aged 0–5.*

for this analysis as information on paternal smoking was not collected at the 1970 interview. In general, rates of admissions to hospital for lower respiratory tract illnesses and bronchitis followed the trend of the mother's smoking rather than the father's, with the highest rates occurring in children whose mothers smoked most heavily, irrespective of the father's cigarette usage. Logistic multiway contingency table analysis confirmed this relation.

Table 1   *Children aged 0–5 admitted to hospital with lower respiratory tract illness according to parental smoking habits*

Daily No of cigarettes smoked by father	Daily No of cigarettes smoked by mother					
	None		1–14		15 or more	
	No studied	% Admitted to hospital	No studied	% Admitted to hospital	No studied	% Admitted to hospital
None	5216	2.7	924	3.0	1198	5.3
1–14	884	2.4	473	3.8	569	8.4
15 or more	1559	2.8	770	3.4	1586	4.5

Table 2   Children aged 0–5 with at least one episode of bronchitis according to parental smoking habits

Daily No of cigarettes smoked by father	Daily No of cigarettes smoked by mother					
	None		1–14		15 or more	
	No studied	% With episodes of bronchitis	No studied	% With episodes of bronchitis	No studied	% With episodes of bronchitis
None	5039	14·5	893	19·3	1049	20·9
1–14	774	14·0	459	14·4	266	27·3
15 or more	1514	16·2	742	19·0	1520	22·4

Maternal smoking had a significant influence (p<0·01) on both admissions to hospital with lower respiratory tract illness and the incidence of bronchitis; paternal smoking had no significant influence on either condition when maternal smoking was taken into account.

There was an overall high collinearity between maternal smoking during pregnancy and postnatal maternal smoking assessed at five years: over 90% of women who smoked in pregnancy were still smoking when their children were 5 years old. To assess whether smoking during pregnancy influenced children's subsequent respiratory health independently of postnatal smoking it was necessary to identify mothers who changed their smoking habits before or after the birth of the study child and compare rates of respiratory illness in their children with those of the ones whose mothers smoked continuously or not at all.

Table 3 shows the rates of bronchitis and admissions to hospital for lower respiratory tract illness according to the mothers' smoking habits. Smoking during pregnancy, but stopping before the child was born, was associated with an increased incidence of all lower respiratory tract illnesses, but smoking only after the birth of the child had no obvious effect on admissions to hospital though an apparent effect on the incidence of bronchitis. Logistic analysis of these data confirmed the highly significant effect of smoking during pregnancy on both rates of admission to hospital (p<0·001) and incidence of bronchitis (p<0·01); postnatal smoking alone had no effect on admissions to hospital and a marginal, though not significant, effect on the incidence of bronchitis.

Because the effect of maternal smoking on children's respiratory health is most obvious in early life,[6] and because our information about postnatal smoking was collected when the children were 5 years old, the effect of varying duration of postnatal smoking was examined. Rates of admissions to hospital were not influenced with smoking during pregnancy remaining highly significant (p<0·001) and duration of postnatal smoking having no significant effect. Rates of bronchitis, however, were found to be highest in children whose mothers smoked both during pregnancy and for most or all of the time from birth to age 5. Significant and independent effects from both smoking during pregnancy (p<0·01) and postnatal smoking (p<0·05) were found on logistic analysis. More than 10% of the information on the duration of postnatal smoking was missing, however, so these results must be assessed with caution.

The mothers were compared for marital state, social class, length of full time education, and age at

Table 3   Children aged 0–5 admitted to hospital with lower respiratory tract illness, or having bronchitis, according to mothers' smoking habits

	No studied	% Admitted in hospital	% With episodes of bronchitis
Smoked continuously	5629	4·4	30·3
Smoked only during pregnancy	493	5·9	18·9
Smoked only after child was born	353	3·1	18·2
Never smoked	5852	2·3	14·0

Table 4   Social data (1970 survey) on mothers according to their smoking habits

	No studied	% In social classes 4 and 5	% Who left school aged <16	% Unmarried	% Aged under 20
Smoked continuously	5629	26·0*	74·9*	7·4	10·8
Smoked only during pregnancy	493	15·1	62·4	7·7	12·3
Smoked only after child was born	353	18·3	64·0	7·6	15·1
Never smoked	5852	18·5	50·4	3·0*	6·5*

*Significantly different from other values in column (p<0·001, partitioned χ^2 analysis).

Table 5 *Percentage of children admitted with lower respiratory tract illness in different age groups according to mothers' smoking habits*

Age at admission (months)	Mother smoked during pregnancy (n=6122)	Mother did not smoke during pregnancy (n=6205)	p Value	Mother smoked when child 5 years old (n=5902)	Mother did not smoke when child 5 years old (n=6325)	p Value
<12	2·07	0·93	<0·001	2·09	0·95	<0·001
12-35	1·83	1·05	<0·001	1·76	1·13	<0·001
35-59	1·14	0·66	<0·01	1·05	0·77	NS

delivery (Table 4). Continuous smokers differed from non-smokers for each of these factors, but those who stopped smoking before birth and those who started smoking postnatally did not differ significantly from each other on partitioned χ^2 analyses. Mothers who smoked continuously differed significantly from the other three groups in social class and educational attainment: non-smokers differed from the other three groups for marital state and age at child's birth. It seems unlikely, therefore, that variation in socioeconomic factors among the four smoking groups explains our results, nor did there seem to be an unexpected effect from paternal smoking: rates of illness in the children among the four groups did not vary significantly when patterns of paternal smoking were considered.

The age at which bronchitis occurred was not known, but the age at admission to hospital for lower respiratory conditions was. Table 5 shows the effect of maternal smoking habits on rates of hospital admission at different age periods during the first five years. Children with repeated admissions were counted only once during each age period. Maximum differences between admission rates for children of smoking and non-smoking mothers occured during the first year of life. There was, however, still a significant difference up to the age of 3 years, and this trend continued up to 5 years. Although there was high collinearity between the two assessments, smoking during pregnancy (those who smoked continuously and those who stopped during pregnancy) had a significantly more persistent effect than subsequent smoking (those who smoked continuously plus those who took up smoking after the birth).

Discussion

These results, as well as confirming previous studies which have shown that parental smoking has a harmful effect on children's respiratory health, suggest that smoking during pregnancy may have a more important and independent effect on the risk of respiratory illness in children than passive exposure to smoking after birth. None of the previous studies on parental smoking and respiratory illness in children has considered a congenital effect from maternal smoking in pregnancy; because of the size and range of CHES, however, it has been possible to examine the effects of both smoking and changing smoking habits. With the application of log linear modelling techniques we were able to assess the prenatal and postnatal components of the overall effect of smoking on children's respiratory illness. In the light of these results earlier studies and their recommendations may require reappraisal.

Rates of admission to hospital for lower respiratory illnesses at least once during the first five years of life were higher in children whose mothers smoked at some time during pregnancy but who stopped before delivery and did not then smoke postnatally, as in children whose mothers smoked in pregnancy and continued to smoke after the birth of the child. Rates of admission to hospital remained low when mothers who did not smoke during pregnancy began smoking subsequently. Smoking after birth did not influence rates of admission to hospital independently of smoking during pregnancy. As far as bronchitis during the first five years of life was concerned, smoking during pregnancy had a major effect but postnatal smoking also seemed to influence rates of illness. Although rates of bronchitis were higher in children of mothers who smoked only during pregnancy and not subsequently than in children whose mothers never smoked, the highest rate of bronchitis was seen in children whose mothers smoked both during pregnancy and during the children's first five years. The need for admission to hospital probably reflects more serious respiratory disease than does reported bronchitis.

The findings concerning the level of maternal smoking support our overall conclusions. Mothers who continued to smoke tended to smoke more with time. Only 30·4% of these mothers were heavy smokers (15 or more cigarettes a day) during pregnancy, whereas 50·5% were five years later. Only 15·0% of those who stopped smoking had been heavy smokers, compared with 27·7% of those who started smoking postnatally. Thus heavier postnatal

smoking did not overcome the apparent harmful effect of smoking during pregnancy.

Rates of admission to hospital were highest in children of mothers who smoked during the first year of life (Table 5). Although there was a strong correlation between the two measures, smoking assessed during pregnancy seemed to have a more persistent effect than postnatal smoking assessed five years later.

These findings suggest that smoking during pregnancy may cause congenital damage to the developing respiratory system, either the bronchial tree or the developing lung vasculature, as has been shown in the umbilical vessels.[19] An alternative explanation for the apparent effect of smoking during pregnancy is that some interference with the immune system might predispose to respiratory infections—a secondary congenital immunodeficiency. Cigarette smoking is immunosuppressive both in vivo and in vitro.[20] Datau et al described abnormalities of polymorphonuclear leucocyte function in children of parents who smoke,[21] and Paganelli et al showed an abnormality in immune function in cord blood from mothers who smoke.[22]

Cigarette smoking during pregnancy has been associated with reduced birth weight, and low birth weight is associated with a wide range of defective immune functions that might predispose to respiratory infection.[23] Low birth weight, although showing a highly significant correlation with rates of both admission to hospital and bronchitis, had its effect independent of maternal smoking.

An additional observation concerns the rate of lower respiratory illness in the offspring of teenage mothers in our study population. These children for various social, environmental, and biological reasons might have been expected to have a high rate of lower respiratory tract illness: they were more likely than children born to older mothers to have low birth weights, to have unmarried mothers of low educational attainment and low social class, to live in poor neighbourhoods, to move frequently, and to have more siblings at the age of 5. Their mothers were more likely than older mothers to be smokers and to be heavy smokers (15 or more cigarettes a day) when the children were 5 years old. These children were, however, no more liable than children of older mothers to bronchitis or to be admitted to hospital.[24] A possible explanation for these paradoxical results was the finding that although teenage mothers were more likely to smoke some cigarettes during pregnancy, they were less likely than older mothers to be heavy smokers during this time, especially those who were under 18 years old when their children were born. Rates of respiratory illness across the whole maternal age

range in general followed rates of smoking during pregnancy and not postnatal smoking.[25]

Many of the data used in this study were collected retrospectively, and so variable maternal recall might have influenced the findings. The large sample size and representativeness of the study population, however, should reduce this effect. The data also reflected the current habits, and are consistent both for reported bronchitis and the more objective variable of admission to hospital. Adequate agreement was found between medical data and parental reports of lower respiratory tract illness resulting in consultations with general practitioners[2] and hospital admission,[26] even though there may be variation between the two sources in exactly what names the respiratory conditions are given.[27] The data used in the present analysis were collected in 1970 and 1975, before there was widespread appreciation of the possible ill effects of parental smoking on children's respiratory health: the questions are thus likely to have been honestly answered.

The accumulated evidence suggests that, whatever the mechanism, exposure to cigarette smoke is bad for children during both intrauterine and subsequent life.

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Editorial Committee

Members of our Editorial Committee usually serve for five years. We thank Dr A S Hunter and Professor J S Wigglesworth. who have retired from the Committee, for their excellent work on behalf of the Journal.

We welcome as new members Dr M J Dillon. Consultant Nephrologist. Hospital for Sick Children, London; Dr I M Hann. Consultant Haematologist. Royal Hospital for Sick Children, Glasgow; Dr J W Keeling. Consultant Pathologist. John Radcliffe Hospital. Oxford, and Dr J F N Taylor, Hospital for Sick Children. London.

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SUMMARY: The incidences of alimentary and respiratory illnesses were observed during the first year of life in 1565 infants born in Tayside during 1980.   Significant correlations $(p<0.05)$ were found between each of these outcomes and parental smoking, maternal age, social class, method of infant feeding, and heating fuels. Multiple logistic regression indicated a significant independent effect of parental smoking was related separately to alimentary and to respiratory outcomes, the relative risks being of similar strength.

Association of infant alimentary and respiratory illness with parental smoking and other environmental factors

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SUMMARY   The incidences of alimentary and respiratory illnesses were observed during the first year of life in 1565 infants born in Tayside during 1980. Significant correlations ($p < 0.05$) were found between each of these outcomes and parental smoking, maternal age, social class, method of infant feeding, and heating fuels. Multiple logistic regression indicated a significant independent effect of parental smoking was related separately to alimentary and to respiratory outcomes, the relative risks being of similar strength.

Said and co-workers[1] were the first to report an association between parental smoking and post-prandial colic and other digestive symptoms in infants. In their study of 253 3-month-old infants, mothers were asked at a routine consultation whether the child cried after feeding and seemed to be in pain. There appeared to be a dose-response relation between parental smoking and reported post-prandial colic, rising from an incidence of 34% in children with non-smoking parents to 90% in children where both parents smoked. Children with one parent who smoked had an intermediate incidence.

This report led us to examine the reported alimentary illness among infants born in Tayside. We examined disease incidence during the first year of life in relation to several potential risk factors including parental smoking.

Subjects and methods

The data were gathered as part of the Tayside Infant Morbidity and Mortality Study.[2] The subjects were the infants of primigravidae who had made an initial booking at any of the Tayside antenatal clinics during 1980. Health visitors interviewed the parents to obtain their ages, social class, ethnic groups, and various aspects of their housing and accommodation including the main methods of cooking and heating. Information on the father's smoking habits and on the mother's smoking habits during pregnancy was obtained at the first antenatal interview. Further information on her smoking during pregnancy was obtained from a postnatal questionnaire completed by the mother while in hospital. As these data were provided by only 80% of the mothers and there was

good agreement between the antenatal and postnatal responses, we classified smoking according to the former source. Current data (unpublished) for Tayside mothers indicate that although during pregnancy smokers reduce the number of cigarettes smoked, few abstain. Among families with smokers we found no trend of increasing infant morbidity with number of cigarettes smoked daily. In the light of these observations we categorised the parents according to whether or not they smoked, categories which could be expected to remain valid during and after pregnancy. A summary record was completed when the child was 1 year of age and included a report on the child's illnesses during the first year of life derived from observations made by the health visitors during their scheduled visits to see the child. A paediatrician verified the diagnostic criteria and consistency.

Disease incidence was defined here as the presence of at least one episode of illness recorded by the health visitor. An episode of respiratory illness was defined as infection of the upper or lower respiratory tract. Alimentary illnesses were mainly diarrhoea or vomiting, or colic. The separate medical conditions were not recorded for the collective diagnoses of respiratory and alimentary illness.

The statistical methods used included chi squared for contingency tables, with partitioning and for trend. Multiple logistic regression and log-linear models were fitted using the computer package GLIM.[3]

Results

A total of 1940 mothers were interviewed, representing over 95% of the mothers of first singleton children who booked at the antenatal clinics. Thirty of the

died—11 stillbirths and 19 infant deaths—leaving 1910 on whom data from the initial interview were available. This figure was reduced to 1565 (82%) infants on whom data for a whole year were recorded, because some families left the region and some health visitors did not return the one-year follow-up information. One or more episodes of alimentary illness were observed in 271 infants (17·3%) and respiratory illness in 494 (31·6%).

Initial tabulation of the data resulted in father's age, cooking type, number of people living in the household, and whether the mother was working during pregnancy being discarded as either not important or containing information implicit in retained variables. The absence of a significant relation between respiratory illness and cooking fuel in this data set has been described in detail elsewhere.[4] Table 1 shows the incidence rates for alimentary and respiratory illnesses according to the main risk factors

of parental smoking, maternal age, bottle feeding, type of heating, and social class. There were missing data for parental smoking, feeding, and father's social class, as indicated.

Among families with smokers there was no trend of increasing infant morbidity with number of cigarettes smoked daily. The parents were therefore classified simply as smokers or non-smokers. Alimentary illness suggested an association mainly with mother's smoking habit, whereas respiratory illness was associated with smoking by either parent. Incidence rates for both alimentary and respiratory illness were consistent with a trend of increasing incidence from families in which neither parent smoked, through those in which the father smoked, to those in which the mother or both parents smoked (χ^2 for trend analysis).

Both alimentary and respiratory illness showed a trend of declining incidence with increasing age of mother, and there was evidence of lower incidence among the breast fed than the bottle fed infants.

The categories of heating type given in table 1 correspond to the main type of heating used in the household. There were significant differences between heating types for respiratory illness only. Alimentary illness was strongly and positively related to social class whereas respiratory illness showed significantly higher rates among manual compared with non-manual groups. Both trends were consistent with a social class gradient; neither showed significant deviation from a linear trend.

MULTIPLE REGRESSION

Because the risk factors were correlated with each other, we analysed their combined influence using multiple regression. For this investigation, in order to reduce the overall number of categories, those individuals with 'not known' or 'other' responses on any variable (social class, heating, father's smoking, feeding) were excluded from the analysis. In addition, social class was recoded simply as non-manual (I, II, IIInm) or manual (IIIm-V). The total number of cases was thereby reduced to 1401.

The incidence of alimentary illness was calculated for each of the cells in the contingency table defined by combination of parental smoking (4 levels), maternal age (3 levels), social class (2 levels), feeding (2 levels), and heating (5 levels).

Of the single factors, parental smoking and maternal age were the most significant (table 2). All the possible two-factor models were fitted, the results of two of which are shown. Stepwise inclusion of the factors suggested that parental smoking and age and possibly heating type gave a satisfactory description of the data. Including extra factors in the model or two factor interaction terms did not give further significant improvement in fit.

Table 1 *Incidence rates (%) of reported alimentary and respiratory diseases in the first year of life according to five risk factors*

Risk factor	No.	Alimentary illness (%)	Respiratory illness (%)
Parents smoking			
Neither	588	14·5	24·8
Father only	338	14·5	33·1
Mother only	177	19·2	38·4
Both	439	22·8	36·4
Not known	23	13·0	34·8
p (chi-square; 3df)		<0·01	<0·001
Maternal age (yr)			
15–	334	22·5	37·7
20–	1088	16·6	30·1
30–	143	10·5	28·7
p (chi-square; 1df)		<0·01	<0·05
Feeding			
Breast	757	15·2	29·2
Bottle	769	19·9	34·5
Not known	39	7·7	20·5
p (chi-square; 1df)		<0·05	<0·05
Heating type			
Central	431	17·4	28·3
Storage	170	11·8	25·9
Coal	215	15·3	27·4
Gas	177	14·1	37·9
Electric	543	20·4	35·0
Others	29	24·1	34·5
p (chi-square; 5df)		<0·10	<0·05
Father's social class			
I	121	13·2	28·9
II	239	11·3	25·1
IIIa	106	18·9	27·4
IIIm	628	16·1	33·1
IV	236	18·6	34·7
V	142	26·1	32·4
Not known	93	28·0	36·5
p (chi-square for trend; 1df)		<0·001	<0·05
p (chi-square: manual v non-manual; 1df)		<0·05	<0·01

Not known categories excluded from χ^2 calculation

Table 2 *Analysis of deviance (approximately distributed as chi-square) for multiple logistic regression models*

Factors fitted	df	Alimentary Illness G^2	Respiratory Illness G^2
None	173	215·2	228·2
Single factor models			
Parental smoking (PS)	170	205·9*	208·9***
Maternal age (MA)	171	206·4*	223·3+
Social class (SC)	172	210·4*	227·7*
Feeding (FE)	172	211·9+	223·4*
Heating (HE)	169	207·1+	211·9**
Two-factor models			
PS + HE	166	199·9−	195·8*
PS + MA	168	200·2+	206·5−
Three-factor models			
PS + MA + HE	164	193·0	193·1

−NS +p<0·10 *p<0·05 **p<0·01 ***p<0·001

174 of the 240 possible cells defined by combinations of the six risk factors actually contained observations. Significance levels are given for single factor models calculated using chi-square test for reduction in G^2 compared with the null model; for 2-factor models G^2 was compared with that for parental smoking.
For alimentary illness, PS + MA + HE is significant compared with (PS + HE)

Table 3 *Regression coefficients (with standard errors) in multiple logistic analysis of alimentary and respiratory illness*

Term	Outcome variables Alimentary Illness	Respiratory Illness
General mean	−1·37 (0·21)	−0·94 (0·19)
Parental smoking		
Neither	0	0
Father	0·00(0·20)	0·36(0·16)
Mother	0·20(0·24)	0·60(0·19)
Both	0·38(0·18)	0·43(0·15)
Heating		
Central	0	0
Storage	−0·49(0·29)	−0·35(0·23)
Coal	−0·23(0·24)	−0·22(0·20)
Gas	−0·43(0·27)	0·35(0·20)
Electric	0·04(0·18)	0·22(0·15)
Maternal age (yr) <20	0	
20−	−0·28(0·18)	−0·24(0·15)
30−	−0·76(0·33)	−0·13(0·24)

The overall goodness of fit test ($G^2 = 193·0$ on 164 df) does not indicate a very good fit ($p = 0·06$). This may be due partly to the large number of cells in the table with small denominators. Thirty-seven of the 174 cells had a denominator of one, and 23 a denominator of two.

The estimated parameters in the regression equation of the log-odds of incidence on parental smoking, type or heating, and maternal age show the positive association with mother's smoking and negative association with age (table 3). The results are in qualitative agreement with the analysis of the crude rates given in table 1. While the families with only fathers who smoked apparently have a similar incidence to non-smoking families, the results are consistent within the limits of sampling variation, with mothers smoking being the main effect and father's smoking habit having a smaller influence. Storage heating, gas and coal fired homes were associated with lower incidences of alimentary symptoms, though the significance levels of these coefficients are low.

A parallel analysis was carried out using respiratory illness in the first year as the outcome variable (table 2). The results of this analysis including other factors have been published elsewhere.[4]

In the analysis of respiratory illness, parental smoking was the most significant factor, while heating type was also significant. None of the remaining factors gave further significant information when included in the analysis, though for comparison with the results obtained for alimentary illness, the equation with parental smoking, age, and heating type was also fitted.

The presence of maternal smoking and, to a lesser extent, heating type as explanatory variables in both respiratory and alimentary illness suggested that it might be possible to fit an equation describing the dependence of both outcome variables on the risk factors simultaneously. Furthermore, one might test for both outcomes on these common risk factors to determine whether the same children tended to experience both types of morbidity.

We can distinguish between (i) where parental smoking has an effect on both alimentary and respiratory diseases, and (ii) where, in addition, the incidences of alimentary and respiratory illnesses are positively correlated. In other words, we can determine whether the risk of respiratory illness is greater if the child suffers from alimentary disease. This may be the case, for example, if there are other shared but unmeasured risk factors present.

It is also desirable to assess whether the observed associations of parental smoking and heating type are consistent between the two outcome variables.

The situation may be modelled according to a method used by Goldstein[5] in analysing longitudinal studies. A five-way contingency table is formed from the two binary outcome factors of respiratory and alimentary illness and the three explanatory (or 'risk') factors identified earlier: parental smoking, maternal age (recorded as <25 years and 25+ years), and heating type.

This contingency table may be modelled using log-linear models.[6] In the simple situation of a single outcome, interest lies in the interaction terms between this factor and the other explanatory factors. These terms and their standard errors may be estimated by maximum likelihood and their significance tested by omitting them from the model and assessing the

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change in goodness of fit statistics. With a binary outcome factor the results obtained are equivalent to the results of a logistic regression of outcome on the explanatory factors.

The log-linear approach can be extended to two outcome factors by defining a contingency table in the same way. First order interactions between each outcome factor and the explanatory factors have similar interpretation to the single outcome model. The interaction term between the two outcome factors measures the tendency of the two outcomes to occur together. Higher order interactions between the two outcome factors and the rest reflect a possible modification of this association by the explanatory variables.

In GLIM, we represent the observed frequencies by a vector and define GLIM 'factors' Y1, Y2, X1, X2, X3 to label the categories of the two outcome and three explanatory variables. Level 1 of Y1 and Y2 denotes absence of the disease, level 2 its presence. For the risk factors, similarly, level 1 denotes the baseline (lowest risk) level, determined from the earlier results. We then fit the following sequence of models:

(1) X1, X2, X3 and all their interactions, with Y1 and Y2 main effects.

(2) Model 1 plus Y1.Y2—allowing for association of the two outcome variables.

(3a) Model 2 plus Y1.X1, Y1.X2, Y1.X3, to represent the main effects of the X factors on Y1.

(3b) Model 3a plus Y2.X1, Y2.X2, Y2.X3, to represent the main effects of the X factors on Y2

(4) Model 3b plus Y1.Y2.X1, Y1.Y2.X2, and Y1.Y2.X3 which denote possible modification of the association between Y1 and Y2 in the presence of X1, X2, and X3 risk factors.

The results of this modelling process showed that the data were consistent with the simpler model 3b without including the outcome interaction terms (table 4). Omitting the RESP.ALIM term from model 3b gave an increase in deviance of only 0·80 (1 df). The original approach of modelling alimentary and respiratory outcomes separately was therefore a

justified alternative, and the coefficients representing the effects of the risk factors on the two outcomes in the combined analysis (table 5) agreed closely with those from the separate regressions (table 3).

An advantage of using the combined model is that we can also test the consistency of the regression coefficients of Y1 and Y2 on one of the explanatory factors, eg, X1. In GLIM, the same analysis as outlined above may be obtained with Y1 and Y2 declared as (0,1) variates instead of two-level factors. If we then compute a new variate YS = Y1 + Y2 and fit model 3 with the Y1.X1 and Y2.X1 terms replaced by YS.X1 we effectively fit model 3b with the Y1.X1 and Y2.X1 interaction terms held equal. Imposing the constraints ALIM.PS = RESP.PS and ALIM.MA = RESP.MA did not increase the deviance significantly ($G^2 = 103.4$; df = 105), suggesting that the effects of PS and MA were consistent between the two outcomes. The resulting coefficients give the logistic regression coefficients on either outcome as:

Only father smoking	0·24(0·13)
Only mother smoking	0·47(0·15)
Both parents smoking	0·46(0·11)
Mothers aged >25 years	−0·14(0·10)

Imposing the further constraint that ALIM.HE = RESP.HE increases the deviance to $G^2 = 109.2$; df = 109. This indicates that the difference between the effects of heating type on the two outcomes might be attributable to sampling variation. However, most of the increase in G^2 appeared to arise from differences between the effects of gas heating on respiratory and on alimentary outcomes.

Discussion

The general finding in our data was that parental smoking was associated with higher reported alimentary and respiratory illness in the first year of

Table 4 *Analysis of deviance for combined log-linear model*

Factors fitted	G^2	df
(1) PS + MA + HE + interactions + RESP + ALIM	152·2	118
(2) + RESP.ALIM	151·9	117
(3a) + RESP.PS + RESP.MA + RESP.HE	118·2	109
(3b) + ALIM.PS + ALIM.MA + ALIM.HE	100·2	101
(4) + RESP.ALIM.(PS + MA + HE)	93·6	93
Model 3b with constraints ALIM.MA = RESP.MA and ALIM.PS = RESP.PS	103·4	105

Table 5 *Estimated coefficients in log-linear analysis of alimentary and respiratory illness*

Term	Alimentary illness	Respiratory illness
Parental smoking		
Neither	0	0
Father only	0·03(0·21)	0·37(0·16)
Mother only	0·25(0·24)	0·61(0·19)
Both	0·45(0·18)	0·45(0·15)
Heating		
Central	0	0
Storage	−0·47(0·29)	−0·36(0·23)
Coal	−0·19(0·24)	−0·22(0·20)
Gas	−0·39(0·27)	−0·53(0·20)
Electric	0·08(0·18)	0·20(0·15)
Maternal age (yr)		
<25	0	0
25-	−0·17(0·16)	−0·12(0·13)

the child's life, the associations being of similar magnitude. This gives some support to the finding by Said *et al* of association between parental smoking and colic, though the effect in our subjects is somewhat diluted by the longer study period and the wider class of alimentary illness.

A mechanism for the association between colic and parental smoking is unclear, though it may be due to a link between taste, smell, and reflex intestinal activity. There is the possibility that the observed association may not be causal but may reflect the fact that parental, and particularly the mother's, smoking habit is associated with the child's social and demographic characteristics, or more probably aspects of their home environment such as quality of care given to the child. For example, mother's smoking might reflect inversely her maternal attitudes and personality and, as a result, the general level of health care provided to the child, including attention and mothering time. However the association with maternal smoking is found fairly consistently in our analysis, despite controlling for other factors. A further analysis in which a finer social class scale was used instead of type of heating resulted in similar estimated effects of smoking, showing that the effect of maternal smoking was resistant to controlling for other variables.

Maternal smoking, maternal education, family living standards, and quality of care provided to the child were included as potential confounding factors in a study in New Zealand[7] primarily aimed at quantifying the effects of breast feeding on respiratory and gastrointestinal morbidity. These factors accounted for some of the crude difference in morbidity rates between breast and bottle fed infants for respiratory illness but not for gastrointestinal illness. The effect of feeding type in our study was fairly small, possibly because it reflected only feeding practice on discharge from hospital, whereas more detailed follow-up information could have given greater importance to this variable.

The evidence against smoking during and after pregnancy as it affects the health of the child is now substantial. Maternal smoking is well known to be associated with low birthweight; it has been shown in a follow-up study to have substantial effects on pulmonary function;[8] parental smoking is associated with frequency of cough and respiratory illness in offspring[6,9-11] and with growth after birth[12,13] as well as the later uptake of the smoking habit.[14,15] This new analysis confirms the finding of Said *et al*,[1] implicating

a further category of ill health associated with passive smoking. Each effect taken above may be small and within physiological limits but, when viewed together, they have an adverse influence on many aspects of child development.

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ABSTRACT. The effect of passive smoking on respiratory symptoms
of children aged 5 to 11 years was investigated in over 4000 English
children and nearly 800 Scottish children participating in the
National Study of Health and Growth in 1982. After adjusting for
associations of respiratory symptoms with age, sex, and a number
of potentially confounding variables, significant associations
were found of wheeze, both occasional and persistent, day or night
cough, and bronchitis attacks with number of cigarettes smoked by
parents at home for English children and for occasional wheeze in
Scottish children. Asthma attacks and cough first thing in the
morning showed positive but not statistically significant
associations in English children. The presence of at least one
condition was statistically significant in both English and Scottish
children. The largest relative risk for exposure to 20 cigarettes
a day compared to no exposure was 1.60 for persistent wheeze in
English children (95% confidence interval 1.17-2.18).

Passive smoking and respiratory conditions in primary school children

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SUMMARY The effect of passive smoking on respiratory symptoms of children aged 5 to 11 years was investigated in over 4000 English children and nearly 800 Scottish children participating in the National Study of Health and Growth in 1982. After adjusting for associations of respiratory symptoms with age, sex, and a number of potentially confounding variables, significant associations were found of wheeze, both occasional and persistent, day or night cough, and bronchitis attacks with number of cigarettes smoked by parents at home for English children and for occasional wheeze in Scottish children. Asthma attacks and cough first thing in the morning showed positive but not statistically significant associations in English children. The presence of at least one condition was statistically significant in both English and Scottish children. The largest relative risk for exposure to 20 cigarettes a day compared to no exposure was 1·60 for persistent wheeze in English children (95% confidence interval 1·17–2·18).

Among the harmful effects postulated for passive smoking is a possible association between parental smoking and respiratory conditions in children, which has been investigated in a large number of studies. A review article[1] concluded that the studies were consistent in suggesting increased infections in children under 1 year of age but inconsistent in older children. As almost all found some effect of parental smoking, the latter conclusion seems to have been due to the lack of a significant dose-response relation in just over half the studies considered.

The studies on older children have varied in the symptoms studied, in the age range of the children, in the proportion of parents who smoked, and in the potentially confounding variables that have been taken into account. A report of a workshop on the effect of passive smoking on children[2] listed nine groups of such variables that it is desirable to take into account. No study has included all of these, and most included only a few variables in one or two of the listed groups. This can be attributed largely to the fact that few[2] of the studies were designed to investigate passive smoking effects, and were opportune analyses on data collected mainly to investigate the relations in children between symptoms and lung function and a variety of environmental factors.

Of even more importance to the detection of a dose-response relation the studies have differed markedly in size and in the measure of passive smoking. The most usual measure was the number of parents smoking, providing lower power to detect a dose-response relation than a measure of the amount smoked. A recent review[3] reported only three studies of young children in which the measure of passive smoking was cigarettes smoked per day, and just one study of older children.

The National Study of Health and Growth, an on-going surveillance study of the health and growth of primary school children in England and Scotland, was also not designed to investigate passive smoking effects. Data on the number of smokers of five or more cigarettes a day in the child's home were collected in 1977 as a confounding variable in a study of the relation of respiratory illness and outdoor air pollution.[4] These data also suggested a negative relation of child's height to number of smokers in the home after adjusting for birthweight.[5] In order to study this association further, data on the number of cigarettes smoked at home by each parent and by the mother during pregnancy, were collected in 1982.[6] No data on lung function were obtained.

Further examination of the 1977 data on English and Scottish children showed a number of statistically significant positive associations of respiratory symptoms with the number of smokers. Given the reasonable sample size, the availability of data for a

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Table 1 *Number of children for whom data on each respiratory condition were obtained and the prevalence (%) of each condition, by sex and country*

Respiratory condition	England				Scotland			
	Boys		Girls		Boys		Girls	
	No	Prevalence %	No	Prevalence %	No	Prevalence %	No	Prevalence %
Chest EVER sound wheezy or whistling	3063	12·6	2870	9·5	572	13·1	563	6·9
Chest wheezy or whistling on MOST days or nights	3046	3·2	2858	2·6	569	4·4	564	2·8
In the last 12 months had: Bronchitis attack(s):	3030	4·0	2852	2·7	570	3·5	565	2·1
Asthma attack(s):	3060	4·2	2862	2·8	568	2·3	567	2·1
Usually coughs first thing in the morning	3048	4·2	2851	4·5	569	5·1	558	5·0
Usually coughs during the day or at night	3036	8·3	2858	7·8	568	11·1	560	8·4

number of potentially confounding variables, and the almost unique data on amount of smoking in the home, it was decided to investigate the dose-response relation of symptoms to passive smoking, using the 1982 data, in children aged 5 to 11 years.

Methods

In 1982 children took part in the study in 22 areas in England and five in Scotland. Data on the child's respiratory symptoms, parental smoking, and family background were obtained from a self-administered questionnaire completed by the child's mother. Triceps skinfold thickness was measured as described elsewhere[7] and was included in the analysis as previously[8] a relation had been shown between respiratory symptoms and this measure of obesity.

Each of six respiratory symptoms or illnesses, given in table 1, was analysed as a dichotomous, ie, present or absent, dependent variable using logistic regression. Any child with a missing value was excluded from the analysis of that symptom. The number of cigarettes smoked per day at home by the mother and father in total, the passive smoking component, and the number of cigarettes smoked per day by the mother during pregnancy with the child were each included as a quantitative variable. Two groups of potentially confounding variables were included in the regression analyses, those treated as quantitative variables and those that were categorical variables. The former group consisted of the child's age, birthweight, triceps skinfold thickness expressed as a standard deviation score,[7] mother's age, and number of siblings. The categorical variables were: child's sex; father's social class, in four groups as non-manual, skilled manual, semi-skilled or unskilled manual, or other; father employed, unemployed or not known; child in one-parent family, two-parent, or not known; presence or

absence of household overcrowding, defined as a ratio of people in the household to number of rooms of at least 1·25; mother's education as highest full-time level in seven groups, none or primary only, secondary or comprehensive school, grammar, technical or commercial college, university, other, or not known. Except as stated missing data excluded a child from the analysis.

Analyses were carried out with all these as independent variables and also with just parental smoking, age, and sex as the independent variables, for England and Scotland separately, and for the two countries combined. Analyses were also carried out for each sex separately and, using the fully adjusted model, with the dependent variable as presence of at least one of the respiratory conditions.

Results

In 1982 there were 8118 children eligible to take part in the study; a questionnaire was returned for 87·8% of these children.

Table 2 *Distribution of cigarettes smoked per day by parents at home in England and Scotland*

No of cigarettes (total smoked by father and mother)	% of parents	
	England	Scotland
0	57·9	59·9
<4	3·4	3·0
5-14	16·9	19·9
15-24	12·4	19·7
25-34	5·2	4·2
>35	4·2	8·4
No of children whose parents are included in this table	5169 (100%)	928 (100%)

Table 3   *Results of logistic regression analyses for England showing the association between respiratory symptoms and passive smoking# from the fully adjusted model*

Respiratory symptom	Regression coefficient ± standard error		
	Boys (N = 2181 to 2246)	Girls (N = 2074 to 2128)	All children (N = 4255 to 4371)
Chest EVER sounds wheezy or whistling	0·008 ± 0·007	0·014* ± 0·008	0·011† ± 0·005
Chest wheezy or whistling MOST days or nights	0·037** ± 0·011	0·010 ± 0·013	0·024** ± 0·008
In the last 12 months had:			
Bronchitis attack(s)	0·004 ± 0·012	0·033* ± 0·013	0·018* ± 0·008
Asthma attack(s)	−0·005 ± 0·012	0·026* ± 0·013	0·009 ± 0·009
Usually coughs first thing in the morning	−0·002 ± 0·012	0·022* ± 0·011	0·012 ± 0·008
Usually coughs during the day or at night	0·007 ± 0·008	0·020* ± 0·008	0·013† ± 0·006
At least one condition	0·008 ± 0·006	0·011 ± 0·007	0·009* ± 0·005

† p < 0·1   * p < 0·05   ** p < 0·01
# parental smoking defined as the total number of cigarettes smoked at home by mother and father together

PREVALENCE OF RESPIRATORY CONDITIONS

Table 1 shows the number of children for whom data were obtained on each respiratory condition, which varied from 86·4% to 87·1% of the total eligible, and the percentage with each condition, by sex and country. The prevalence of each condition was greater in boys than in girls but differed little between England and Scotland.

DISTRIBUTION OF PASSIVE SMOKING

Data on parental smoking were available for 75·1% of children. The distributions of the number of cigarettes smoked per day by the parents at home are given in table 2 for children in England and Scotland. Smoking by parents was more prevalent in Scotland than in England.

RELATION OF RESPIRATORY CONDITIONS TO PASSIVE SMOKING

After exclusions for missing data, primarily in respiratory symptoms or parental smoking, the number of children available ranged from 4337 (63·4%) to 4371 (63·9%) for England and from 766 (60·90%) to 771 (61·3%) for Scotland. Table 3 shows the relation of six respiratory conditions to passive smoking for English children as estimated from the logistic regression analysis, adjusted for all the potentially confounding variables listed above. For all children parental smoking was most strongly positively associated with 'chest wheezy or whistling on most days or nights' (p < 0·01) and also significantly associated (p < 0·05) with 'usually coughs during the day or night', 'chest ever sounds wheezy or whistling', and bronchitis attacks in the last 12 months. The relation was positive for the other two conditions. Although results appeared to show some differences between boys and girls, no significant difference, as assessed from an interaction term in the model, was found in the relation of passive smoking except for asthma (p < 0·05), which showed a positive association (p < 0·1) with parental smoking in girls, and a non-significant negative relation in boys. The relation of prevalence of at least one of the conditions was just significant (p < 0·05) for all English children.

For Scottish children, who were fewer in number than the English children, the only significant relation of an individual condition to parental smoking was found for 'chest ever wheezy' (p < 0·01). However the prevalence of at least one condition was significantly related to parental smoking (p < 0·05).

Results are given for England and Scotland separately as the relation of 'chest ever wheezy' and 'wheeze most days or nights' to passive smoking was found to differ significantly between the two countries (p < 0·05). 'Wheeze most days or nights' showed a relation to passive smoking only in England, whereas 'chest ever wheezy' showed a stronger relation to passive smoking in Scottish children than in English, of similar size to that for persistent wheeze in English children.

EFFECTS OF ADJUSTMENT FOR CONFOUNDING VARIABLES

Table 4 shows the relation between passive smoking and each respiratory condition adjusted only for age for boys and girls separately, and for age and sex for all English children. Comparison with table 3 shows that in most cases adjustment for the potentially confounding variables generally increased the standard errors so there was a reduction in statistical significance, the notable exceptions being 'chest wheezy or whistling most days or nights' in boys, and bronchitis attacks in girls for which the regression coefficient increased considerably on adjustment. For

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Table 4 Results of logistic regression analyses for England showing the association between respiratory symptoms and parental[#] smoking for the model adjusted only for age (and sex for all children)

Respiratory symptom	Regression coefficient ± standard error		
	Boys (N = 2181 to 2246)	Girls (N = 2074 to 2128)	All children (N = 4255 to 4371)
Chest EVER sound wheezy or whistling	−0·002 ± 0·006	0·013* ± 0·006	0·005 ± 0·004
Chest wheezy or whistling MOST days or nights	0·023* ± 0·009	0·033** ± 0·009	0·028*** ± 0·007
In the last 12 months had			
Bronchitis attack(s)	−0·002 ± 0·010	0·022* ± 0·010	0·008 ± 0·007
Asthma attack(s)	−0·014 ± 0·010	0·018* ± 0·010	0·000 ± 0·007
Usually coughs first thing in the morning	0·001 ± 0·010	0·021* ± 0·008	0·012* ± 0·006
Usually coughs during the day or at night	0·015* ± 0·006	0·026*** ± 0·006	0·021*** ± 0·004
At least one condition	0·005 ± 0·005	0·012* ± 0·006	0·008* ± 0·004

N = the range of the number of children in the six analyses
* p<0·1   * p<0·05   p<0·01   p<0·001
[#] See footnote to Table 3.

Table 5 Estimates of prevalence (%) of respiratory symptoms and relative risk for children* of parents smoking no cigarettes, 10 and 20 cigarettes at home per day, based on the fully adjusted model for all children

Respiratory condition	Prevalence % (relative risk compared to non-smoking parents)		
	Cigarettes smoked at home by parents		
	0	10	20
Chest wheezy or whistling on MOST days or nights	2·8	3·5 (1·27)	4·5 (1·60)
Bronchitis attack(s) in the last 12 months	3·9	4·7 (1·18)	5·5 (1·40)
Usually coughs during the day or night	7·7	8·7 (1·13)	9·8 (1·27)
At least one condition	17·4	19·3 (1·08)	20·8 (1·16)

* Given for boys aged 8 years, with no siblings, in a two parent family, father employed and social class IIIB, mother's smoking in pregnancy 0, home not overcrowded, mother aged 32 and educated at a secondary or comprehensive school, triceps skinfold standard deviation score 0, birthweight 3000 g.

all Scottish children, adjusting only for age and sex, significant associations were found between passive smoking and 'chest ever wheezy' (p<0·01), 'usually coughs during the day or night' (p<0·05), and prevalence of at least one condition (p<0·01).

ESTIMATES OF RELATIVE RISK

Table 5 gives examples of prevalence of respiratory conditions and relative risk (in parentheses) estimated from the regression coefficients in the fully adjusted model for the three conditions showing the largest associations with passive smoking in all English children. Compared with children whose parents do not smoke the relative risks were around 1·2 for children whose parents smoke 10 cigarettes a day in total at home, and from 1·3 to 1·6 for those whose parents smoke 20 a day. They are of necessity given for fixed values of the other independent variables but would not differ markedly for different values of these variables. The relative risk of at least one condition is

lower, only just significantly different from 1·0 at the 5% level, but shows the estimated increase in the percentage of children suffering some respiratory symptom at the given levels of parental smoking.

Discussion

A number of statistically significant positive associations were found between respiratory conditions in children and number of cigarettes smoked per day at home by their parents, but not consistently for all symptoms or in both countries. The result also differed to some extent from those found in the 1977 data, in which the passive smoking variable, number of smokers of at least five cigarettes a day in the home, was significantly associated (p<0·05) with all six conditions except bronchitis in the last 12 months. The analyses of the two years' data differed in the confounding variables taken into account, the use of gas for cooking and population density being

included in the 1977 analysis, but not maternal smoking in pregnancy or mother's education or age. They were similar in the age range of the children, in sample size, and in the wording of the questions about respiratory conditions.

Inevitably, other studies have differed in the symptoms or illnesses studied and in the exact questions asked. However the largest study with a similar age range,[9] in which 10 106 children aged 6 to 10 years were involved, found highly significant associations ($p < 0.001$) between cough for three months or more of the previous year and wheeze most days or nights with maternal smoking, and a less significant association ($p < 0.01$) of bronchitis with maternal smoking, broadly in line with our findings.

Other studies have also found significant positive associations between persistent cough and parental smoking,[10-12] and, although not statistically significant, a relative risk of 4.9 for persistent wheeze was found for children exposed to a smoker at home compared to those never exposed in a study of 626 children under 15 years.[12]

The only other study[13] to include 'cough first thing in the morning' found a positive association ($p < 0.05$) in 12 year old girls after allowing for the child's own smoking. Many studies of passive smoking have included non-persistent wheeze, with various definitions, and some asthma or bronchitis. About half of those obtained significant positive associations, and the rest non-significant associations. However, few studies have included all four symptoms of wheeze, cough, asthma, and bronchitis. Apart from the question of prime importance being whether passive smoking causes any harmful effect to children of primary school age, the nature of the effect being a secondary consideration, the symptoms are not manifestations of distinct diseases. Analysis of single symptoms may fail to detect a real increase in the prevalence of a condition. In particular, an effect of passive smoking increasing symptoms of asthma may be missed if only a question about asthma is included due to underdiagnosis in many children with wheeze[14,15] and the fact that cough may be the only presenting symptom.[16]

No data were available on active smoking by the children as the questionnaire was completed by a parent. However, even in the oldest age group and on the assumption that smoking by the child is strongly associated with parental smoking, the prevalence of active smoking would be too small to account for the differences in prevalence of respiratory symptoms. Dobbs and Marsh[17] reported a prevalence of regular smoking, defined as 'at least one cigarette a week', of 1% and 0% in first year secondary school boys and girls respectively, in England in 1982, and 5% and 3% in Scotland. Of the groups of other confounding

variables that have been suggested[2] that are relevant to children's symptoms as reported by the mother, those of other indoor pollutants are probably the most important ones not included in the analysis of the 1982 data. In the analysis of 1977 data the use of gas for cooking, an important source of nitrogen dioxide in the home,[18] did not eliminate positive associations of respiratory symptoms with passive smoking.

Parental symptoms are on the list of potentially confounding variables,[2] and there is no doubt that a child's symptoms show a relation to these.[9,10,12,19] However, as many of the symptoms of smokers will be a result of their smoking, adjustment for parental symptoms could remove a real effect of parental smoking on a child's health.[20] Of the few studies in which the adjustment had been made the largest[9,20] still found positive associations between child's cough and wheeze and maternal smoking in over 10 000 6-10 year old children. Lebowitz[12] in a much smaller study, found statistical significance of an association removed by the adjustment. Schenker et al[19] found a positive association between chest illness on at least three days in the last year which persisted on adjustment for parental respiratory disease, but found no association before or after adjustment in chronic cough, phlegm or wheeze in 4000 children aged 5 to 14.

Studies have varied in the prevalence of respiratory conditions and in the percentage of parents smoking. While low values of either may lead to statistically insignificant results in the presence of a real effect, the most important variation in the studies has been in sample size. The majority of studies provide no information on the amount smoked by parents. For children of two parents who smoke the estimated relative risk of the respiratory conditions studied was less than two compared to children of non-smoking parents in almost all studies.[3] The conclusion that emerges is that if there is a real effect of passive smoking on the respiratory health of children aged 5 to 11 years, then it is a small one, and a large study is required for a high probability of its detection. Although results for the smaller sample of Scottish children were not significantly different from those for English children, except for wheeze, a significant relation was found only for 'chest ever wheezy' and at least one condition. For English children the largest relative risk was for persistent wheeze, of 1.60 in children whose parents smoked a total of 20 cigarettes a day (95% confidence interval 1.17-2.18) and 1.16 (1.00-1.34) for any symptom. The USA six cities study[9] found a relative risk of 1.3 for persistent wheeze in 6 to 10 year old children whose mothers smoke 20 cigarettes a day.

As the association is probably less strong than that for children under 1 year, it is to be expected that secondary school children would show a weaker, or no

association of symptoms with passive smoking. We have therefore confined consideration of the literature to studies including broadly similar age groups. All four studies[9][13][21][22] that we have identified with an analysis of data for 6000 or more children in a similar age range to those in our 1982 English sample have shown at least one significant positive association with passive smoking. The two largest[21][22] also showed a dose-response relation. Our data have supported the hypothesis of an effect of parental smoking on children of this age. Scepticism could be removed further only by a study of several symptoms in at least 6000 children, including all potentially confounding variables as recommended,[2] with a quantitative measure of passive smoking by the child.

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Chen, Y. "Synergistic Effect of Passive Smoking and Artificial Feeding on Hospitalization for Respiratory Illness in Early Childhood" <u>Chest</u> 95: 1004-1007, 1989.

ABSTRACT. The synergism of passive smoking and artificial feeding on hospitalization for respiratory illness in early childhood was examined among 2,227 subjects born in the last quarter of 1983 in Chang-Ning District, Shanghai, People's Republic of China. The eligible families were visited by the trained interviewers. A loglinear model shows no interaction on a multiplicative scale between these two factors on the frequency of hospitalization for respiratory illness during the first 18 months of life. However, the synergism of passive smoking and artificial feeding on the consequence was detected by using Rothman's approach that these two synergistic agents worked together producing a detrimental effect much more than that expected by their separate actions. These data suggested that it is more important to stop smoking in the families where the infants were artificially fed.

Synergistic Effect of Passive Smoking and Artificial Feeding on Hospitalization for Respiratory Illness in Early Childhood*

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The synergism of passive smoking and artificial feeding on hospitalization for respiratory illness in early childhood was examined among 2,227 subjects born in the last quarter of 1963 in Chang-Ning District, Shanghai, People's Republic of China. The eligible families were visited by the trained interviewers. A loglinear model shows no interaction on a multiplicative scale between these two factors on the frequency of hospitalization for respiratory illness during the first 18 months of life. However, the synergism of passive smoking and artificial feeding on the consequence was detected by using Rothman's approach that these two synergistic agents worked together producing a detrimental effect much more than that expected by their separate actions. These data suggested that it is more important to stop smoking in the families where the infants were artificially fed. (Chest 1989; 95:1004-07)

> ICD = International Classification of Disease; ID = incidence density; IDR = incidence density ratio

Our earlier papers presented that household exposure to tobacco smoke and artificial feeding are both important risk factors of hospitalization for respiratory illness during a child's first 18 months of life.[1,2] The combined effect of these two factors seems even greater than that expected by their separate actions.[3] Although this picture is not statistically significant in the above study due to limited sample size, it was hypothesized that there may be synergism between these two agents that the infants artificially fed are more vulnerable to be hospitalized for respiratory illness caused by passive smoking in early childhood. In this analysis, the data of Chang-Ning Epidemiologic Study of Children's Health[3] was further examined to identify the potential synergism of passive smoking and artificial feeding on hospitalization for respiratory illness during the first 18 months of life.

METHODS

The study covers the total area of Chang-Ning District, Shanghai, People's Republic of China. All 2,315 live birth babies born in the last quarter of 1963 in this area were selected as the study population. The survey was conducted during the period from March to June 1965 when the children just reached the age of one and half years. Each questionnaire was administered and recruited to each child's home by trained interviewers. This questionnaire asked about dates and causes of hospitalization from birth to 18 months, smoking habits of parents and other household individuals and type of feeding of the child. The questionnaire also included questions on sociodemographic data, baby's characteristics, residential conditions and household environmental exposure, parental education, and all family members' chronic respiratory diseases during the child's first 18 months of life. Among the eligible sample, 2,227 questionnaires were completed, with response rate of 96 percent. Selected characteristics of the population are shown in Table 1.

The diagnosis of hospitalization for respiratory illness include ICD (9th revision)[4] codes 460, 462-466, 480, 485-487, 492, 493, 786.2. The children studied were divided into three passive smoking

Table 1—Frequency of Selected Characteristics of the Population

	No.	%	Mean	SD
Sex				
Boys	1155	51.9		
Girls	1072	48.1		
Multiple birth				
No	2184	98.1		
Yes	43	1.9		
Feeding type				
Breast or mixed	1483	66.6		
Artificial	744	33.4		
Day-care nursery				
No	1720	77.2		
Yes	507	22.8		
Father's education				
University	200	9.6		
Secondary	1999	89.6		
Primary	28	1.3		
Coal used for cooking				
No	990	44.0		
Yes	1247	56.0		
Adult(s) in family with chronic respiratory disease				
Yes	396	17.8		
No	1831	82.2		
Cigarettes smoked daily by family member(s)				
None	481	21.6		
1-19	993	44.6		
20+	753	33.8		
Birth weight, kg			3.2	0.44
Maternal age at birth, yr			28.2	3.01
Average income, yuan			38.8	9.51
Number of rooms			2.5	1.20
Total living area, m²			25.0	19.46
Average living area per person, m²			5.4	4.32

groups according to total number of cigarettes smoked daily by family members: none, 1 to 19 cigarettes/day, and 20+ cigarettes/day; and two feeding groups: a completely artificially fed group which consisted of the infants who had never been breast-fed and a group of breast-fed infants which consisted of those who were fully or partially breast-fed at any time in the first ten months of life.

Incidence density (ID) was used to measure the frequency of hospitalization.[?] The point and interval estimation for Rothman's index S was used to measure the synergistic effect of passive smoking with artificial feeding upon hospitalization on an additive scale.[?] Confounding factors were adjusted by stratified analysis. Denoting the standardized incidence density for risk indicator category i, j as SID_{ij}, the Rothman's index of the joint risk-indicator-specific sets of strata is computed by

$$S_{ij} = \frac{SID_{ij} - SID_{oo}}{SID_{io} + SID_{oj} - 2SID_{oo}},$$

and taking for the pooled point estimate

$$S = \frac{W_{ij} \cdot S_{ij}}{W_{ij}},$$

$$W_{ij}^* = W_{ij}E_{ij}.$$

Here, E_{ij} is the corresponding theoretical joint effect under independence, and W_{ij} is the weight for that category. The standard error of the natural logarithm of S was evaluated by using first order Taylor series approximation.[?]

RESULTS

There were 1,746 smoking families, 78.4 percent of the total, in which (786) only the father smoked, in 261 only another family members smoked, and in 699 both father and other family members smoked. No mothers who were smokers were found. The crude IDRs were 2.5 for 20+ cigarettes per day group and 1.7 for 1 to 19 cigarettes per day compared to nonsmoking families. The influence of passive smoking on the other diagnostic categories is not statistically significant. The independent effects of passive smoking have been detailed elsewhere.[?]

In this study, artificial feeding is another important risk factor of hospitalization for respiratory illness in early childhood. One third of the children were totally artificially fed up to ten months. The frequency of hospitalization for respiratory illness among artificially fed children is about two times higher than that among breast-fed ones (IDR = 1.9, p<0.01). Table 2 presents the incidence density of hospitalization for respiratory illness during the first 18 months of life by smoking status of family members and children's feeding type. It shows that the risk increased with the increasing of smoking amount by family members among these artificially fed children more rapidly than that among the breast-fed ones. It seems that the artificially fed children are more susceptible to respiratory illness due to household exposure to cigarette smoke. Figure 1 pictures a framework of the combined effect of passive smoking with artificial feeding on the inpatient admission for respiratory illness during the first 18 months of life.

Table 3 shows the IDRs of hospitalization for respi-

Table 2 — *Incidence Densities of Hospitalization for Respiratory Illness in Early Childhood by Passive Smoking and Feeding Type*

Feeding Type	Cigarettes Smoked Daily by Family Members			
	None	1-19	20+	Total
Breast or mixed				
Cases	13	34	35	82
Person-years	445.5	1011.0	768.0	2224.5
ID (/year)	0.0292	0.0336	0.0456	0.0369
Artificial				
Cases	9	36	35	80
Person-years	276.0	478.5	361.5	1116.0
ID (/year)	0.0326	0.0752	0.0968	0.0717
Total				
Cases	22	70	70	162
Person-years	721.5	1489.5	1129.5	3340.5
ID (/year)	0.0304	0.0470	0.0620	0.0485

ratory illness of various groups combined passive smoking with feeding type compared with the breast-fed children without exposure to cigarette smoke in the household before and after adjusting covariates including sex, birth weight, and father's educational status. Rothman's approach detected a significant synergistic effect of these two factors on the hospitalization for respiratory illness during the first 18 months of life. The pooled point estimate of Rothman's index S is 3.8 with the 90 percent confidence interval from 1.24 to 11.34 after adjusting the confounding factors. Analysis by using loglinear model shows the interaction on a multiplicative scale between these two factors is not statistically significant.

DISCUSSION

This report depicts the joint effect of passive smoking and artificial feeding on the hospitalization for respiratory illness during the first 18 months of life that passive smoking worked together with artificial feeding would produce a detrimental effect much
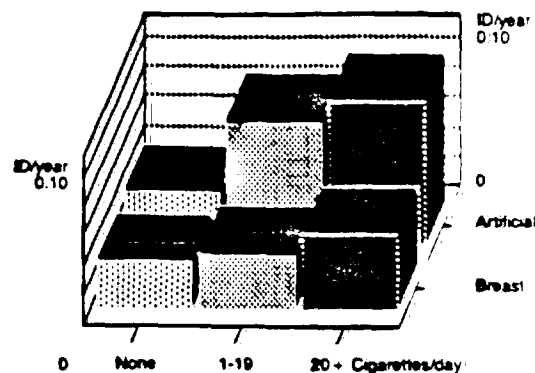

FIGURE 1. Combined effect of passive smoking and artificial feeding on hospitalization during first 18 months of life.

Table 3—Synergism of Passive Smoking and Feeding Type on Hospitalization for Respiratory Illness in Early Childhood

Cigarettes smoked daily by family member(s)	Feeding type	Unadjusted IDR	Unadjusted S_{ij}	Adjusted* IDR	Adjusted* S_{ij}
None	Breast or mixed +	1.00		1.00	
	Artificial	1.12		1.10	
1-19	Breast or mixed	1.15		1.22	
	Artificial	2.56	5.90	2.91	5.97
20†	Breast or mixed	1.56		1.64	
	Artificial	3.32	3.41	3.37	3.20

*Adjusted variables included: sex, birth weight and father's education.
†Reference group.

more than that expected by the separate action of these two factors.

The reports concerning respiratory infection and artificial feeding have been conflicting. Several studies have shown a significant association between them,[7-15] but not others.[16-20] Although information needed to evaluate the conclusions was not included in most of studies. Methodologic problems might explain a part of these differences.[21-23] The results of this report based on a larger study population add weight to our earlier conclusion that artificial feeding increased a risk of hospitalization for respiratory illness in early childhood.

Although many studies pictured an increased risk of respiratory infection associated with passive smoking and artificial feeding, none explicitly described the interaction between them with the health outcome. The possibility of interaction was mentioned only in the study by Watkins et al[8] besides our earlier report.[9] After examining the type of feeding and respiratory infection in the first year of life, in the study by Watkins et al,[8] they found that high-risk infants appeared to benefit more from breast-feeding. The estimated incidence of respiratory infection in artificially fed infants, predicted by fitting a general interactive model to the data, ranged from 42 percent in boys with more than two siblings, whose parents smoked and mothers reported cough and phlegm to 4.9 percent in girls with no siblings neither of whose parents smoked nor reported cough or phlegm. In the breast-fed infants, the comparable estimates were 30 percent to 2.9 percent. The difference between 12 percent predicted attributable risk reduction for high-risk infants and 2 percent for low-risk infants reflects the interaction between type of feeding and mixed effect of sex, siblings, parental smoking status, and maternal respiratory troubles. But the interactive effect of parental smoking with type of feeding was not isolated in this study.

In this study, the child's sex is another predictor of hospitalization for respiratory illness. The IDR was 0.063/year in boys vs 0.042/year in girls. The synergistic effect of passive smoking and artificial feeding is evident in both groups. The incidence density ratios were 3.2 in artificially fed boys whose family members smoked, compared with breast-fed boys, and 1.2 in those only whose family members smoked and 1.1 in those only artificially fed, and they were 3.2, 1.5 and 1.1, respectively, in girls.

For epidemiologic studies of the health effects of infant feeding, various potential sources of bias are considerable. In this study, all infants were classified dichotomously. The breast-feeding group consisted of infants who were completely breast-fed during the first ten months of life, some who received only a few feedings of human milk, and others who fit between these two extremes. The effect of artificial feeding on the hospitalization for respiratory illness is probably underestimated.[2,19] Although the duration of breast-feeding can be alternatively used to evaluate the protective effect of human milk feeding, selection bias will probably emerge.[5] Since infant feeding is a one-way street, the children are often placed on artificial feeding when they fail to thrive and become ill, and children who are breast-fed exclusively for a prolonged period of time are likely to be extremely healthy.[23-25] As Kramer said, the investigator must often navigate between the Scylla and Charybdis.[5] Dichotomous classification of infant feeding in this report, for another reason, can keep the number of each subgroup sufficient for stratified analysis.

In most studies from developed countries, it seems a knotty problem to distinguish between the effect of maternal smoking during pregnancy and the effect of environmental exposure to cigarette smoking.[26] However, young women smoking is very rare here, and no young mother who smoked was detected in this study and in others as well.[1,26,27] Other potential sources of bias have been discussed in detail elsewhere.[3]

Many studies have explored the possible mechanisms of the protective effect of breast feeding and the detrimental effect of passive smoking on the health outcomes.[28-30] Breast milk is considered the best infant food due to its cleanliness, nutrition and content of a number of antiinfectious agents which make infants able to resist the invasion of certain pathogenic agents. Environmental tobacco smoke can be a substantial contributor to the level of indoor air pollution concentrations of the respiratory particles benzene, acrolein, N-nitrosamine, pyrene, and carbon monoxide.[30] Although the evidence is not yet convincing for the synergism of passive smoking and type of feeding, this will not stop us from tendering advice that it is more important to keep the artificially fed children from tobacco smoke pollutants.

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Corbo, G.M., Feuciarelli, F., Foresi, A., De Benedetto, F. "Snoring in children: association with respiratory symptoms and passive smoking" BMJ 299:   1491-1494, 1989.

ABSTRACT: Objective -- To investigate the relation between snoring and various respiratory symptoms in passive parental smoking. Design -- Data were collected by questionnaire. Setting -- Primary schools in Guardiagrele and Francavilla in the Abruzzi region in central Italy. Subjects -- 1,615 Children aged 6-13 years were categorised [sic] according to whether they snored often; occasionally apart from with colds; only with colds; or never. Results -- 118 Children were habitual snorers and 137 were reported to snore apart from when they had colds. Never snorers (n = 822) were significantly older than children in other categories. Snoring was significantly associated with rhinitis, production of cough and sputum, previous tonsillectomy, and passive parental smoking. Of the habitual snorers, 82 were exposed to passive smoking. The prevalence of habitual snoring increased significantly with the number of cigarettes smoked by parents (from 5.5% in moderate smoking households to 8.8% in heavy smoking households). Conclusions -- Snoring is quite common in children. The dose-effect relation of smoking and snoring shown in this study adds weight to a further adverse effect of parental smoking on children's health.

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Snoring in children: association with respiratory symptoms and passive smoking

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Abstract

Objective—To investigate the relation between snoring and various respiratory symptoms and passive parental smoking.

Design—Data were collected by questionnaire.

Setting—Primary schools in Guardiagrele and Francavilla in the Abruzzi region in central Italy.

Subjects—1615 Children aged 6-13 years were categorised according to whether they snored often; occasionally apart from with colds; only with colds; or never.

Results—118 Children were habitual snorers and 137 were reported to snore apart from when they had colds. Never snorers (n=822) were significantly older than children in other categories. **Snoring was significantly associated with rhinitis, production of cough and sputum, previous tonsillectomy, and passive parental smoking. Of the habitual snorers, 82 were exposed to passive smoking. The prevalence of habitual snoring increased significantly with the number of cigarettes smoked by parents (from 5·5% in moderate smoking households to 8·8% in heavy smoking households).**

Conclusions—Snoring is quite common in children. **The dose-effect relation of smoking and snoring shown in this study adds weight to a further adverse effect of parental smoking on children's health.**

Introduction

Although snoring is often regarded as trivial, it has been associated with hypertension, heart disease, and stroke, and it is considered to be the first step towards the development of the sleep apnoea syndrome. Heavy snorers can suffer obstructive apnoea and alveolar hypoventilation during sleep as well as an increase in pulmonary and systemic arterial pressures.

Bloom and coworkers have found that cigarette smoking, obesity, male gender, and age are risk factors for snoring and that snoring is associated with cough and sputum production. Snoring is common in adults (24-71% of men and 14-52% of women), and the prevalence tends to increase with age.

Snoring during childhood has been investigated only in selected clinical samples, and it has been found to be associated with sleep apnoea and related symptoms such as excessive daytime somnolence, hyperactivity, and behavioural or intellectual changes. These observations suggested that chronic snoring in a child should prompt appropriate investigation and treatment. Despite evidence of the clinical consequences of snoring no data are available regarding the prevalence of snoring in a general population of children.

We investigated the prevalence of snoring in a general population sample of children aged 6-13 years and the occurrence of snoring in association with age, sex, respiratory symptoms, and parental passive smoking.

Methods

The study was conducted in two towns in the Abruzzo region (Guardiagrele and Francavilla) in central Italy. We studied the overall population of schoolchildren in the first degree (aged 6-11 years) (1907 subjects: 964 boys and 943 girls) and in the second degree (aged 10-13 years) (455 subjects: 235 boys and 220 girls). The rate of compliance was 97%. To avoid possible bias towards non-snorers we excluded from the analysis children who had been sleeping alone because the prevalence of snoring in these children was significantly lower than in children sharing a bedroom with siblings or parents (3·6% *v* 7·3%; $\chi^2=10·7$; $p=0·0011$). The excluded sample (747 subjects: 389 boys and 358 girls) did not differ as regards age, sex, respiratory symptoms, and smoking habits of the parents from the examined group (1615 subjects: 810 boys and 805 girls, aged 6-13 years). Data on snoring, respiratory symptoms, and parental smoking were obtained from a modified American Thoracic Society children's questionnaire, which was completed by the parents.

DEFINITIONS

The question concerning snoring was: "Does your child ever snore?" On the basis of the answer four categories were formed: (1) never; (2) only with colds; (3) occasionally apart from with colds; and (4) often. Children included in the last category were defined as habitual snorers.

Asthma was defined as an affirmative response to a question about whether the child had been told that he or she had asthma by a doctor. Rhinitis was defined in terms of response to the following question: "Has your child ever had rhinitis (stuffy and running nose, itchy eyes, sneezing)?" Cough and phlegm were defined as cough or phlegm that occurred apart from with colds.

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Lastly, parents were asked if their child had had a tonsillectomy because of throat infections.

Households in which both parents had never smoked were classified as non-smoking; those with either one parent or both parents who were current smokers (that is, currently smoking at least one cigarette each day or having stopped smoking within the past 12 months) were classified as smoking. Smoking households with smokers were classified into moderate (summed total for both parents of less than 20 cigarettes each day) and heavy smokers (summed total of 20 cigarettes each day or more). Duration of parental smoking during the child's lifetime was also recorded.

STATISTICAL ANALYSIS

The mean age of the children in the four categories of snoring was compared by variance analysis and orthogonal comparisons." The categories were analysed with reference to sex and parental passive smoking and also to asthma, rhinitis, cough and phlegm, and tonsillectomy by giving an arbitrary score to each category (never=-3, only with colds=-1, sometimes apart from with colds=1, and often=3), and the significance of linear trends was tested." We present the odds ratio referring to habitual snorers compared with non-snorers with 95% confidence intervals." As smoking has been implicated as a risk factor for snoring" stratified techniques were utilised to adjust for the effect of passive smoking." We calculated 95% confidence intervals for the Mantel-Haenszel weighted odds ratio." Children who snored only with colds and children who snored sometimes apart from colds were excluded from the stratified analysis.

The prevalence of habitual snoring compared with that of never snoring was compared in children from non-smoking households and households with moderate smokers and heavy smokers by the χ test for trend."

Weights of zero were assigned to the non-smoking group and the median numbers of cigarettes smoked to the two smoking groups 10 and 22, respectively. A p value <0.05 was considered significant.

Results

In all, 118 children (7.3%; 59 boys and 59 girls) were habitual snorers and 137 (8.5%; 67 boys and 70 girls) were reported to snore apart from when they had colds (table I). Mean age differed significantly in the four snoring categories (variance analysis $F=7.27$; $p=0.0002$). Never snorers were significantly older than children in other categories ($F=19.7$; $p<0.001$). There was no difference in the prevalence of snoring between girls and boys ($\chi=0.43$).

There was a relation between prevalence of snoring and several respiratory symptoms (table II). Snoring was significantly associated with rhinitis ($\chi=23.9$; $p<0.0005$); rhinitic children were more than twice as likely to be habitual snorers (odds ratio=2.93; 95% confidence interval 1.70 to 5.00). The relation between rhinitis and habitual snoring was not affected by the presence of passive smoking (table III).

Asthmatic children were more likely to be snorers than other children ($\chi=5.6$; $p<0.025$), but risk of habitual snoring did not achieve significance (odds ratio=1.88; 0.98 to 3.50). Cough and sputum production were associated with an increased prevalence of snoring ($\chi=11.06$; $p<0.001$) (table II). The risk of habitual snoring was also significantly increased (odds ratio=1.84; 1.09 to 3.10). Cough and sputum production was still related to habitual snoring after adjusting for passive smoking (table III), but the association was stronger in children whose parents did not smoke (2.52; 1.02 to 6.07) than in children exposed to passive smoking (1.56; 0.79 to 3.03).

Prevalence of snoring was also increased in children who had had tonsillectomy ($\chi=14.05$; $p<0.0005$) (table II). The prevalence of habitual snoring was increased about twofold (12.6% v 6.5%; odds ratio= 2.66; 1.60 to 4.47). The relation of tonsillectomy to habitual snoring was not affected by the presence of passive smoking (table III), but the risk of habitual snoring was higher in children from smoking house-

holds (3.21; 1.70 to 5.98) than in children from non-smoking households (1.53; 0.49 to 4.49).

Of the total sample, 959 children (59.4%) had either one parent or both parents who currently smoked (table IV). Snoring was closely related to passive parental smoking. Children of smoking parents were more likely to be snorers than children whose parents never smoked ($\chi=18.5$; $p<0.0005$). Of the 118 habitual snorers 82 (69%) were exposed to passive smoking (1.85; 1.20 to 2.89). Complete data on the daily amount of cigarettes smoked by parents were available for 922 of the 959 children (96%) (table IV).

TABLE I—*Prevalence of snoring in children (n = 1615) according to age and sex*

	Never	Only with colds	Apart from with colds	Habitual
No (%) of children	822 50.9	538 33.3	137 8.5	118 7.3
95% Confidence interval %	48 to 53	31 to 36	7 to 10	6 to 9
No (%) boys	398 49.1	286 35.3	67 8.3	59 7.3
95% Confidence interval %	46 to 52	32 to 38	6 to 10	6 to 9
No (%) of girls	424 52.7	252 31.3	70 8.7	59 7.3
95% Confidence interval %	49 to 56	28 to 34	7 to 11	6 to 9
Mean SD age (years)	9.73 (1.75)	9.31 1.75	9.33 1.78	9.39 1.78
95% Confidence interval %	9.6 to 9.86	9.16 to 9.46	9.03 to 9.64	9.06 to 9.72

TABLE II—*Prevalence of snoring in children (n = 1615) according to presence of various respiratory symptoms*

	Never n=622	Only with colds n=538	Apart from with colds n=137	Habitual n=118	χ Trend	p Value	Odds ratio*	Confidence interval
No (%) with rhinitis	69 8.4	76 14.1	23 16.8	35 29.7	23.90	<0.005	2.93	1.71 to 5.00
95% Confidence interval %	6 to 10	11 to 17	10 to 23	21 to 38				
No (%) with asthma	59 7.2	54 10.0	14 10.2	15 12.7	5.60	<0.025	1.88	0.98 to 3.50
95% Confidence interval %	5 to 9	7 to 12	5 to 15	7 to 19				
No (%) with cough or phlegm	100 12.2	102 19.9	25 18.2	24 20.3	11.06	<0.001	1.84	1.09 to 3.10
95% Confidence interval %	10 to 14	16 to 23	12 to 25	13 to 27				
No (%) who had had tonsillectomy	79 9.6	87 16.2	15 10.9	26 22	14.05	<0.0005	2.66	1.60 to 4.47
95% Confidence interval %	8 to 12	13 to 19	6 to 16	15 to 29				

*Never snoring v habitual snoring.

TABLE III—*Relative risk (odds ratios) of habitual snoring for children with rhinitis, cough or phlegm and tonsillectomy after adjustment for passive smoking*

	Children from smoking households	Children from non-smoking households	All children	χ*	p Value
Rhinitis	2.78	3.22	2.92	16.9	<0.0005
95% Confidence interval	1.42 to 5.43	1.23 to 8.22	1.75 to 4.85		
Cough or phlegm	1.56	2.52	1.84	5.23	<0.025
95% Confidence interval	0.79 to 3.03	1.02 to 6.07	1.12 to 3.01		
Tonsillectomy	3.21	1.53	2.62	13.90	<0.0005
95% Confidence interval	1.70 to 5.98	0.49 to 4.49	1.59 to 4.32		

*Mantel-Haenszel test.

TABLE IX — *Prevalence of snoring in children 1615 according to smoking habits of parents*

	Never	Only with colds	Apart from with colds	Habitual	χ² Trend	p value	Odds ratio*	Confidence interval
No % non-smokers	368 44.8	215 40.0	37 27.0	36 30.5				
95% Confidence interval %	41 to 48	36 to 44	20 to 34	22 to 39				
Total No % smokers	454 55.2	323 60.0	100 73.0	82 69.5	18.5	<0.0005	1.95	1.2 to 2.8
95% Confidence interval %	52 to 58	56 to 64	66 to 80	61 to 78				
No % moderate smokers†	209 26.1	153 29.1	47 34.8	37 32.2	13.4	<0.0005	1.81	1.08 to 3.00
95% Confidence interval %	23 to 29	25 to 33	27 to 43	24 to 41				
No % heavy smokers†	225 37.9	158 42.4	51 58.0	42 53.8	14.8	<0.0005	1.91	1.16 to 3.1
95% Confidence interval %	34 to 42	37 to 47	48 to 68	43 to 65				

*Never snoring : habitual snoring
†Daily number of cigarettes smoked by parents was known for 922 children.

All of the parents who smoked had started smoking before the birth of the child. Prevalence of snoring was increased in children both from moderate smoking households (χ^2=13.4; p<0.0005), and from heavy smoking households (χ^2=14.8; p<0.0005). Prevalence of habitual snoring increased with the amount of cigarettes smoked (8.8% in children from heavy smoking households (odds ratio=1.91; 1.16 to 3.10) compared with 8.6% (1.81; 1.08 to 3.00) and 5.5% in children whose parents were moderate smokers or never smokers, respectively). This dose related effect of passive smoking was significant (χ^2=9.04; p<0.005).

Discussion

We found that respiratory symptoms such as rhinitis and cough or phlegm production, a previous tonsillectomy, and passive parental smoking were associated with an increased prevalence of snoring. As far as we know this is the first report of the prevalence of snoring in a general population sample of children. The prevalence of snoring was 7.3% in the overall sample. The accuracy of reporting snoring can be influenced by several factors. Firstly, reported snoring is arbitrarily defined.[1][8][9] Secondly, questionnaire data may underestimate the true prevalence of snoring.[9] Thirdly, as the subject is usually not aware of snoring answers mostly depend on the parent, and this bias can be further increased in children whose parents do not sleep in the same room. We have been able to reduce this bias only by excluding from the analysis children sleeping alone. The actual prevalence of snoring in children may be even higher than that observed.

Prevalence of snoring tended to decrease with age. As snoring depends on pharyngeal size[11] older children, because of larger pharyngeal cross sectional areas, may have a lower risk of snoring than younger children. In our sample prevalence of snoring was equal in boys and girls whereas a predominance of snoring in men is a common finding in adult populations.[3][9][10] This discrepancy may be due to the prepubertal age of our sample. Testosterone has an apnoea promoting effect,[12] whereas progesterone is a respiratory stimulant[13] and may enhance activity of the pharyngeal dilator muscles.[14] Thus these hormones may play respectively a positive and an inhibitory role in the development of snoring in men and in women. Moreover, it has been shown that prevalence of snoring increases progressively in men after 20 years of age, whereas in women this increase occurs only after 40 years of age.[1]

Rhinitis was associated with an increase in prevalence of snoring. Bloom and coworkers failed to find this relation in adults.[11] Rhinitis has, however, been found more commonly in snoring children than in snoring adults,[3] and it has been shown that high nasal airflow resistance can increase both the incidence of snoring[15] and of obstructive sleep apnoea.[16][17]

A weak association was observed between snoring and asthma, but the risk of habitual snoring was not significantly increased in children with asthma. This result agrees with previous findings in an adult population.[1] We observed a close association between snoring and cough or sputum production. Bloom and co-workers reported the same association in an adult population.[11] After adjustment for passive smoking the relation was still significant. Chronic inflammation may result in a narrowing of pharyngeal size, leading to an increased risk of snoring.

A previous tonsillectomy was related to an increased risk of habitual snoring. This association was stronger in children exposed to passive smoking. This finding agrees with a previous study, which reported an association between parental smoking and tonsillectomy.[18]

The association between passive smoking and snoring was highly significant, and we observed a dose-effect relation between the number of cigarettes smoked by parents and the prevalence of habitual snoring. Smoking has been found to be a risk factor for snoring,[19] and the risk is related to the amount of cigarettes smoked.[6] Moreover, in former smokers the prevalence of snoring is dependent on the time since stopping.[6] These data strongly suggest a chronic effect of smoking on the upper airways. As snoring depends on pharyngeal size, smoking can provoke mucosal oedema and inflammation, resulting in a narrowing of the pharynx. This mechanism, which has been hypothesised in snoring adults who smoke,[6] can also operate in children exposed to passive parental smoking since birth.

In conclusion, our findings show that snoring is quite common in children and is associated with the presence of rhinitis or cough and sputum production. Also it is closely related to passive parental smoking. The dose-effect relation of smoking and snoring strengthens this association. This report puts forward a further adverse effect of passive parental smoking on their children's health. Longitudinal studies should be conducted to assess the course of snoring in childhood related to the development of hypertension, cardiac disease, and the sleep apnoea syndrome.

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Consequences and treatment of ovarian failure after total body irradiation for leukaemia

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Abstract

Objective—To assess the incidence and severity of physical and psychosexual symptoms in young women due to ovarian failure caused by total body irradiation for leukaemia and the women's response to hormone treatment.

Design—Postal questionnaire and interview.

Setting—Leukaemia unit of oncology hospital.

Patients—Consecutive series of 46 English speaking women who had developed ovarian failure after total body irradiation and bone marrow transplantation as treatment for leukaemia.

Results—Of the 36 responders, 33 reported some symptoms, vaginal dryness being the most common (29). This profoundly affected sexual function. Although 22 women had had sexual intercourse within six months after treatment, 16 were less interested in and 18 experienced difficulties with sexual intercourse. Anxieties about sterility, femininity, and appearance were common and reduced self confidence. Almost half reported that they had changed their social habits and restricted their social activities. Treatment seemed effective in abolishing symptoms in 24 women, but vaginal dryness remained a problem in three. Two women failed to respond and intercourse remained impossible.

Conclusions—Such patients are vulnerable and access to gynaecologists and endocrinologists soon after treatment would be valuable. The optimal treatment regimen and the long term benefits of treatment have yet to be established.

Introduction

Total body irradiation and bone marrow transplantation have recently become established treatments for certain types of leukaemia in younger patients. Because of the systemic nature of the disease, no attempt can be made to shield the gonads. Consequently, nearly all women develop amenorrhoea and permanent ovarian failure. As over half are likely to survive long term, recognition of the consequences of total body irradia-

tion and premature ovarian failure are of great importance.

While there has been a recent expansion in our knowledge of the incidence and aetiology of all causes of premature ovarian failure, little is known about the consequences. Various authors have commented on the presence of hot flushes, night sweats, and atrophy of the lower genital tract in patients with premature ovarian failure, but some of these studies included patients who subsequently regained ovarian function spontaneously (and even became pregnant) and clearly, therefore, did not have irreversible ovarian failure. Furthermore, few previous studies have investigated the impact of oestrogen deficiency on sexual function and none on self esteem and social behaviour. We believe that such additional information is vitally important in clinically managing all patients with irreversible premature ovarian failure irrespective of aetiology.

We present data on some of the early consequences of ovarian failure and the effects of hormone therapy in a group of 36 women previously treated with total body irradiation and bone marrow transplantation for leukaemia.

Patients and methods

Forty six English speaking patients who had received total body irradiation and bone marrow transplantation at the leukaemia unit at the Royal Marsden Hospital were sent a questionnaire, to which 36 responded. All patients had received conditioning treatment with cyclophosphamide and total body irradiation or melphalan and total body irradiation. The questionnaire referred to symptoms and concerns experienced by the patients in the six months after treatment.

Of those who responded to the questionnaire, 34 were referred to the unit from hospitals elsewhere in the United Kingdom (from as far afield as Cornwall in the south to the Orkney islands in the north); the two other patients were local. At the time of treatment the average age was 25·7 years (range 14·3 years to 42·6 years) and the mean time between treatment and

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ABSTRACT: The contribution of parental smoking to wheezing in children was studied in a subset of all British births between April 5 and 11, 1970 (N=9,670). Children of smoking mothers had an 18.0 per cent cumulative incidence of post-infancy wheezing through 10 years of age, compared with 16.2 per cent among children of nonsmoking mothers (risk ratio 1.11, 95% CI: 1.02, 1.21). This difference was confined to wheezing attributed to wheezy bronchitis, of which children of smokers had 7.4 per cent, and those of nonsmokers had 5.2 per cent (risk ratio 1.44, 95% CI: 1.24, 1.68). The incidence of wheezy bronchitis increased as mothers smoked more cigarettes. After multiple logistic regression analysis was used to control for paternal smoking, social status, sex, family allergy, crowding, breast-feeding, gas cooking and heating, and bedroom dampness, the association of maternal smoking with childhood wheezy bronchitis persisted. Some of this effect was explained by maternal respiratory symptoms and maternal depression, but not by neonatal problems, the child's allergic symptoms, or paternal respiratory symptoms. There was a 14 per cent increase in childhood wheezy bronchitis when mothers smoked over four cigarettes per day, and a 49 per cent increase when mothers smoked over 14 cigarettes daily.

Parental Smoking and Post-Infancy Wheezing in Children: A Prospective Cohort Study

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Abstract: The contribution of parental smoking to wheezing in children was studied in a subset of all British births between April 5 and 11, 1970 (N = 9,670). Children of smoking mothers had an 18.0 per cent cumulative incidence of post-infancy wheezing through 10 years of age, compared with 16.2 per cent among children of nonsmoking mothers (risk ratio 1.11, 95% CI: 1.02, 1.21). This difference was confined to wheezing attributed to wheezy bronchitis, of which children of smokers had 7.4 per cent, and those of nonsmokers had 5.2 per cent (risk ratio 1.44, 95% CI: 1.24, 1.68). The incidence of wheezy bronchitis increased as mothers smoked more cigarettes. After multiple logistic regression analysis was used to control for paternal smoking, social status, sex, family allergy, crowding, breast-feeding, gas cooking and heating, and bedroom dampness, the association of maternal smoking with childhood wheezy bronchitis persisted. Some of this effect was explained by maternal respiratory symptoms and maternal depression, but not by neonatal problems, the child's allergic symptoms, or paternal respiratory symptoms. There was a 14 per cent increase in childhood wheezy bronchitis when mothers smoked over four cigarettes per day, and a 49 per cent increase when mothers smoked over 14 cigarettes daily. (*Am J Public Health* 1989; 79:168–171.)

Introduction

Children are passive victims of the effects of tobacco smoke from their surrounding environment, resulting in multiple adverse health outcomes.[1-3] Passive smoking has been associated with respiratory infections and symptoms in infants and young children.[4-9] Some studies have suggested an association between parental smoking and wheezing or other respiratory symptoms of older children,[10-14] but other investigations have disputed this relationship.[15-17] A dose effect has been reported,[4,6,12,18-21] although this has been inconsistent and often crudely measured.[8] Parental smoking has also been associated with decreased pulmonary function and lung growth in children.[11,14,19,22-25]

The mechanism of effect of passive smoking on childhood reactive airway disease is not clear. Sidestream tobacco smoke may be directly toxic to the lungs of children. Alternatively, or additionally, the respiratory effects of passive smoking may be mediated by other factors to which children of smokers may be exposed, such as infection,[10,13,26,27] allergy,[15,28] stress,[29] or neonatal respiratory problems.[23]

In order to address some of these unresolved issues, we studied the relationship of cigarette smoking by either or both parents with report of post-infancy wheezing in a large, representative British national cohort.

Methods

The Child Health and Education Study began as a national survey of all births in Great Britain during the week of April 5-11, 1970.[30] Information was collected by midwives during the first postpartum week. At 5 years of age, the cohort was reevaluated by trained health visitors via maternal interviews. Additional parental interviews, medical examinations, and educational evaluations were carried out at age 10.

Maternal smoking behavior was surveyed at each interview, including the duration of smoking from pregnancy through age 10 of the child and the usual dose of cigarettes per day during each period. We asked about the use of cigarettes, pipes, or cigars by the father. The amount smoked by the mother was categorized on the birth questionnaire as 0, 1-4, 5-14, 15-24, and 25 or more cigarettes per day. These categories were applied to doses reported at children's ages 5 and 10, from the continuous measures of amount smoked (there was considerable preference for multiples of five in reporting of dose). In trend analyses, means of each of the first three smoking categories were used: 2.5, 9.5, and 19.5; 29.5 cigarettes per day was used for the highest smoking category.

Outcome data were obtained from maternal interviews when the children were 10 years old. At that time, parents were asked: "Has the child *ever* had one or more attacks or bouts in which there was wheezing or whistling in the chest?" If the reply was positive, they were asked: "What were these thought to be due to?" (. . . asthma, wheezy bronchitis, or other cause, with multiple responses permitted); parents were then asked at what ages the wheezing occurred. Wheezy bronchitis is a common diagnosis in Great Britain, although its clinical distinction from asthma is not clear.

Other variables were selected for study after review of published investigations or parental smoking and other factors related to childhood respiratory symptoms and disease. These included sex of the child, social status of the family (represented by a standardized variable derived from factor analysis of social items when the cohort was 5 years old), crowding in the home (total persons/total rooms), number of siblings (total, older and younger), dampness in the child's bedroom, whether gas was used for cooking and/or heating, child's own smoking at age 10, whether the child was breast fed at least one month, history of allergy in the child or family, neonatal respiratory problems, symptoms of chronic cough or phlegm for over three months in each parent, and a measure of maternal depression (derived from a 24-item Malaise Inventory[31]). Family allergic history was determined at the time the child was age 5 by a report of asthma, eczema, or hay fever in either natural parent. A positive allergic history in the child was defined as a report of eczema or hay

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fever before 5 years of age. Neonatal respiratory problems were defined by a history of any breathing difficulties during the first week of life.

Chi-square, multiple logistic regression, and factor analyses were done using SAS software.[32,33] Confidence intervals on risk ratios[34] and on odds ratios determined from multiple logistic regression[35] were calculated using published methods. Attributable risk calculations were done using methods described by Lilienfeld.[36]

Results

We studied prospectively 11,776 children born between April 5–11, 1970 and their families, obtaining data at birth, and at ages 5 and 10 years. Of this population, 9,953 (84.5 per cent) were singleton births, living throughout with their natural mothers, whose primary language was English, and who were ethnic Europeans. In 836 of these households (8.4 per cent), there was no father figure. There were 5,113 boys (51.4 per cent).

The 9,670 children whose mothers had known smoking information comprise the cohort for the remaining analyses. Of these mothers, 4,855 (50.2 per cent) smoked cigarettes at some time between their pregnancy and the child's age 10. Cigarette smoking was reported at some time by 5,128 fathers in homes with a father figure (56.2 per cent). In addition, 866 (9.5 per cent) of fathers smoked pipes or cigars only.

There were 1,774 children (17.8 per cent) who were reported to have wheezed by 10 years of age. Of these, 112 reported wheezing only before one yer of age; the remaining 1,662 were classified by their parents as having asthma, wheezy bronchitis, or other reasons for wheezing. The relationship of post-infancy wheezing to maternal smoking at any time between pregnancy and child's age 10 (dichotomized) is presented in Table 1. Smoking was associated with post-infancy wheezing in the entire group of children (risk ratio 1.11, 95 per cent CI = 1.02, 1.21). This smoking relationship was limited to the subgroup stated to have had wheezy bronchitis (risk ratio 1.44, 95 per cent CI = 1.24, 1.68). Subsequent analyses relate only to this outcome.

Unadjusted relationships of maternal and paternal smoking with child's wheezy bronchitis are shown in Table 2. The effect of maternal smoking was stronger when fathers also smoked, but these mothers also smoked more cigarettes per day; during pregnancy, 12.5 per cent smoked over 14 cigarettes per day, compared with 4.5 per cent when fathers were nonsmokers. In the homes with no father figure, there was a higher cumulative incidence of wheezy bronchitis.

Wheezy bronchitis was reported to have started before age 5 in 72 per cent of affected children (compared with 65 per cent of those with asthma). The amounts that the mother smoked at child's birth and age 5 years were equally strongly

related to the risk of wheezy bronchitis. Thus, the mean dose of cigarettes per day between the reported amounts at birth and 5 years was used in subsequent dose analyses. The cumulative incidence of wheezy bronchitis by amount smoked by the mother is presented in Table 3. The incidence of wheezy bronchitis increased progressively from 5.2 per cent in nonsmokers to 8.9 per cent among children whose mothers smoked over 24 cigarettes per day, but this dose-effect trend among smokers was not statistically significant.

Wheezy bronchitis was inconsistently related to the duration and period of maternal smoking (Table 4). Those mothers who smoked throughout the study period (from pregnancy through child's age 10) also smoked more cigarettes; their children had a risk ratio of 1.52 (95 per cent CI = 1.27, 1.82) for wheezy bronchitis compared with nonsmokers. The category of mothers who only smoked in both postnatal periods was most strongly related to childhood wheezy bronchitis, although only 12 cases were exposed in this group.

Multiple logistic regression was used to estimate the effects of several factors of post-infancy wheezy bronchitis contrasted with no history of wheezing. The final model included maternal smoking between child's birth and age 5 years with four dose levels; paternal smoking in three categories: cigarette smoking, pipe or cigar smoking only, or father absent from the home; social status, sex of the child, family history of allergy, crowding, breast-feeding, gas cooking or heating, and bedroom dampness. The included social status items after factor analysis were: father's highest educational qualification, father's occupational social class, mother's highest educational qualification, economic level of the neighborhood, telephone in the home, and ownership/rental of home. Highly correlated, redundant variables (e.g., number of siblings) were substituted by more specific mea-

TABLE 2—Cumulative Incidence of Wheezy Bronchitis in Ages 1–10 by Parental Smoking

| Maternal Smoking | Paternal Smoking (Number with wheezy bronchitis) | | | | |
	No	Cigarettes	Pipe/ Cigar	Father Absent	N
No	.051 (110)	.050 (93)	.052 (27)	.066 (18)	4815
Yes	.066 (59)	.076 (238)	.064 (20)	.083 (44)	4855
Total	.055 (169)	.067 (331)	.056 (47)	.077 (62)	9670
Risk Ratio of Maternal effect	1.29	1.52	1.23	1.26	
(.95 CI)	(.95, 1.75)	(1.20, 1.92)	(.70, 2.15)	(.74, 2.14)	

TABLE 1—Post-Infancy Wheezing to Age 10 by Maternal Smoking at any Time

| Reason for Wheezing | Affected Number | Cumulative Incidence | | Risk Ratio (.95 CI) |
		Smokers	Nonsmokers	
Wheezy bronchitis	825	.074	.052	1.44 (1.24, 1.68)
Asthma	282	.028	.029	.96 (.77, 1.22)
Other reason	632	.064	.067	.96 (.83, 1.11)
Combinations of above	123	.013	.013	1.00 (.71, 1.41)
Total	1662	.180	.162	1.11 (1.02, 1.21)

TABLE 3—Cumulative Incidence Rate of Wheezy Bronchitis at Ages 1–10 by Maternal Smoking Dose

| | Average cigarettes per day at birth and 5 years | | | | |
	None	1–4	5–14	15–24	>24
Cumulative Incidence Wheezy Bronchitis	.052	.066	.075	.081	.089
Number Children*	4815	925	2450	991	169
Rate Difference	—	.013	.023	.029	.037

Chi-square (trend) = 1.876, p = 0.17
*240 smoking mothers did not smoke at child's birth or age 5 years; 80 had incomplete dose reporting.

TABLE 4—Incidence of Wheezy Bronchitis (WB) by Period of Maternal Smoking

Pregnancy	Child's Age 0-5	Child's Age 5-10	N	# WB	Cumulative Incidence WB	RR WB	95% CI
n	n	n	4815	250	.052	—	
y	y	y	3302	260	.079	1.52	1.27, 1.82
y	y	n	538	35	.065	1.25	0.87, 1.80
y	n	y	307	20	.065	1.25	0.79, 2.00
y	n	n	164	11	.067	1.29	0.70, 2.39
n	y	y	107	12	.112	2.16	1.19, 3.93
n	y	n	197	15	.076	1.46	0.86, 2.50
n	n	y	240	10	.042	0.80	0.43, 1.51

y = Smoked during pregnancy, or at least three years during interval
n = Did not smoke in pregnancy, or less than three years during interval
RR = Risk ratio

sures (e.g., crowding). Variables unrelated to smoking or wheezing were not included.

The interaction between maternal smoking and the following variables were estimated by both bivariate and multivariate analyses: sex, maternal depression, child allergy, parental allergy, neonatal respiratory distress, breast-feeding, gas cooking, gas heating, crowding, social status, or paternal smoking. The effect of maternal smoking on wheezy bronchitis showed little difference among the levels of any of these factors. Thus, the final multiple logistic models excluded interaction terms.

As Table 5 shows, the dose relationship with maternal smoking appeared to plateau at 15–24 cigarettes per day when all potential confounders were controlled. Male sex, low social status, family allergy, and bedroom dampness, when controlled for maternal smoking, were related to wheezy bronchitis.

Several variables were examined as potential mediators of the smoking effects by adding each separately to the full analytic model, including neonatal respiratory problems, child allergy, and parental respiratory symptoms. These mediating effects were strongest among children whose

TABLE 5—Child's Wheezy Bronchitis by Age 10 Years and Maternal Smoking: Multiple Logistic Regression

# cig/day* (N)	Odds ratios vs nondiseased children (95% CI) controlled for covariates**
None	1.00
1–4 (925)	1.27 (.95–1.70)
5–14 (2450)	1.43 (1.16–1.78)
15–24 (991)	1.49 (1.13–1.97)
>24 (169)	1.49 (.85–2.63)

*Average of amount between birth and age five
**Covariates in model, multivariate odds ratio (95% CI):

Paternal cigarettes	1.05 (.85, 1.29)
Paternal pipe/cigar	1.05 (.75, 1.46)
Father absent	1.06 (.81, 1.43)
Male child	1.39 (1.16, 1.64)
Family allergy	1.48 (1.22, 1.78)
Crowding	0.91 (.71, 1.17)
Bedroom dampness	1.67 (1.31, 2.14)
Not breast fed	1.22 (.97, 1.53)
Gas cooking/heating	1.03 (.86, 1.23)
Social status factor	0.90 (.81, .99)

mothers smoked over 24 cigarettes per day: the maternal smoking effect was reduced (from 1.49 to 1.32) when maternal respiratory symptoms were controlled; parental symptoms exerted no such effect, despite the stronger independent contribution of fathers' report of cough or phlegm to the child's symptoms. A smaller reduction in effect (to 1.36) was evident when maternal depression was included in the analysis. An increase in the effect (to 1.61) was seen when child allergy was held constant. Neonatal respiratory problems showed no mediating effect.

If mothers smoking over four cigarettes per day had not smoked, we estimate that 13.8 per cent of the total burden of wheezy bronchitis in this population would not have occurred.

Discussion

In this large, representative national cohort of British children followed from birth, 18 per cent were reported to wheeze by 10 years of age. A subgroup of these children (those whose symptoms were attributed by their mothers to wheezy bronchitis) were at increased risk of post-infancy wheezing when their mothers were smokers. Paternal smoking did not contribute independently to the risk of wheezy bronchitis, perhaps because young children spent more time with their mothers. Recent changes in parental work and child care patterns may alter these relationships.

Is tobacco smoke directly toxic to children's lungs, or are its effects attributable to other factors? Parents who smoke have more respiratory symptoms themselves and may transmit infections to their children.[10,26,27] Additionally, children may imitate the respiratory symptoms of their parents. We found that report of maternal cough or phlegm resulted in some attenuation of the relationship of maternal smoking with the child's wheezy bronchitis; paternal symptoms showed no such relationship. This finding is consistent with mediation of some of the effect of maternal smoking on the child's wheezing by maternal respiratory symptoms; it also is consistent with maternal smoking jointly causing maternal symptoms and the child's wheezy bronchitis, or with more frequent reports of wheezy bronchitis in children of smoking mothers with respiratory symptoms. A substantial portion of childhood wheezy bronchitis was unexplained by these mediating factors, either due to actual toxicity of sidestream tobacco smoke or unexamined mediating factors.

Passive smoking was related only to wheezy bronchitis and not to reported asthma or wheezing for other reasons. We do not know what clinical characteristics led to the perceived diagnosis of wheezy bronchitis in these children. Several investigators have suggested that asthma and wheezy bronchitis are clinically and pathologically indistinguishable, and that they are both manifestations of reactive airway disease.[37,38] The distinct patterns of association of different categories of wheezing with parental smoking found in this cohort may represent true differences between various forms of wheezing.[39] Alternatively, children exposed to tobacco smoke may have been labeled disproportionately as having wheezy bronchitis by health care providers because of earlier age of onset than expected for asthma, relative absence of other atopic symptoms, or awareness of early published reports of an association between passive smoking and bronchitis in childhood.

Reliance on parent report of smoking and retrospective report of childhood wheezing may add uncertainty to our findings.[8,24] However, the causal relationship between pas-

sive smoking and childhood reactive airway disease is supported here by consistency with previous investigations, temporal coherence of the sequence of exposure and symptoms, a dose-response gradient, and biologic plausibility.[40] Our data do not reveal a specific period of vulnerability to the effects of passive smoking. Further follow-up of this cohort is in progress and may add to our understanding of the effects of passive and active smoking on the natural history of reactive airway disease.

We estimate a 49 per cent increase in the prevalence of childhood wheezy bronchitis by age 10 when mothers smoke more than 14 cigarettes per day, when compared with children of nonsmoking mothers. Perhaps as much as 14 per cent of wheezy bronchitis in this population can be attributed to maternal smoking of over four cigarettes per day. These findings add evidence of the public health hazards of cigarette smoke to those involuntarily exposed.

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SUMMARY: Results are presented from a second cross-sectional assessment of the association of air pollution with chronic respiratory health of children participating in the Six Cities Study of Air Pollution and Health.   Air pollution measurements collected at quality-controlled monitoring stations included total suspended particulates (TSP), particulate matter less than 15 um (PM_{15}) and 2.5 um (PM_{2-5}) aerodynamic diameter, fine fraction aerosol sulfate (FSO_4), SO_2, O_3, NO_2.   Reported rates of chronic cough, bronchitis, and chest illness during the 1980-1981 school year were positively associated with all measures of particulate pollution $(TSP, PM_{15}, PM_{2-5},$ and $FSO_4)$ and positively but less strongly associated with concentrations of two of the gases $(SO_2$ and $NO_2)$.   Frequency of earache also tended to be associated with particulate concentrations, but no associations were found with asthma, persistent wheeze, hay fever, or nonrespiratory illness. No associations were found between pollutant concentrations and any of the pulmonary function measures considered $(FVC, FEV_1, FEV_{0-75}$ and MMEF).   Children with a history of wheeze or asthma had a much higher prevalence of respiratory symptoms, and there was some evidence that the association between air pollutant concentrations and symptom rates was stronger among children with these markers for hyperreactive airways.   These data provide further evidence that rates of respiratory illnesses and symptoms are elevated among children living in cities with high particulate pollution.   They also suggest that children with hyperreactive airways may be particularly susceptible to other respiratory symptoms when exposed to these pollutants.   The lack of association between pollutant concentrations and measures of both pulmonary flow and volumes suggests, however, that these increased rates of illness are not associated with permanent loss of pulmonary function, at least during the preadolescent years.

Effects of Inhalable Particles on Respiratory Health of Children[1-4]

DOUGLAS W. DOCKERY, FRANK E. SPEIZER, DANIEL O. STRAM, JAMES H. WARE, JOHN D. SPENGLER, and BENJAMIN G. FERRIS, JR.

Introduction

A recent report (1) from the Six Cities Study of Air Pollution and Health described a strong association between frequencies of chronic cough, bronchitis, and chest illness in preadolescent schoolchildren and concentrations of particulate and sulfur oxide air pollution in six communities in the eastern United States. Illness and symptom rates were higher by approximately a factor of two in the community with the highest air pollution concentrations compared with the community with the lowest concentrations. No association was found, however, between air pollution concentrations and two measures of pulmonary function, FVC and FEV_1. Because the health data were gathered between 1974 and 1980, only three pollutant variables, total suspended particulates (TSP), the sulfate fraction of TSP (TSO_4), and sulfur dioxide concentrations (SO_2), were consistently available for this analysis. These measurements were gathered from stations operated by a variety of public and private agencies. Analysis of limited data on spatial and temporal variability of air pollution concentrations and respiratory health within the six cities found an association between total sulfate (TSO_4) concentrations and respiratory illness and symptom rates, but not with TSP or SO_2.

These results raised several issues requiring further investigation. (1) To what extent could these results be replicated using air pollution measurements gathered under standardized procedures established as part of the Six Cities Study? (2) Was the respiratory health status of study children associated with either of two measures of size-fractionated particulate matter, aerodynamic diameter less than 15 µm (PM_{15}) and less than 2.5 µm ($PM_{2.5}$)? Did ozone (O_3) or nitrogen dioxide (NO_2) concentrations have a direct effect on respiratory health or modify the associations with other pollutants? (3) Could associations be found between air pollution concentrations and potentially more sensitive measures of small airways impairment ($FEV_{0.75}$ and MMEF) obtained from digitized analysis of the spirometric tracings? (4) Could sensitive subgroups of the study population be identified?

This study investigated each of these issues by analyzing the respiratory health of the original cohort of the school children reexamined during the 1980-1981 school year, a period during which all elements of the study's air pollution measurement program, including size-fractionated particle measurements, were available in all six cities.

Methods

Populations Studied and Survey Procedures

The cohort of school children has been described elsewhere (1-3). Briefly, the children were initially seen as first- and second-graders attending schools in study communities during the enrollment period between 1974 and 1979. Each child had had an annual follow-up examination consisting of a respiratory symptom questionnaire completed by a parent and a spirometric examination performed at school. Health data used in this report were collected during the 1980-1981 school year. Three cities were visited between September and December, 1980: Watertown, MA; St. Louis, MO; and Portage, WI. And three were visited between January and April, 1981: Kingston-Harriman, TN; Steubenville, OH; and Topeka, KS.

Five respiratory illness and symptom responses obtained from the questionnaire were considered: bronchitis, cough, chest illness,

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wheeze, and asthma (4). Bronchitis required a doctor's diagnosis in the last year; chronic cough was defined as being present for 3 months in the last year; chest illness required restriction of activities of 3 days or more. Persistent wheeze was defined as wheeze apart from colds or for most days or nights in the last year. Asthma required the reporting of a doctor's diagnosis.

Three symptoms not expected to be related to air pollution were also considered: earache, hay fever, and nonrespiratory illness or trauma that restricted activities for 3 days or more.

The spirometric examination has been described elsewhere (5). Briefly, the examination was performed using a water-filled recording spirometer (Survey Spirometer; Warren E. Collins, Braintree, MA) with the child in a sitting position without a noseclip. Each tracing was examined in the school by the local study coordinator. Those judged acceptable by standard criteria (4) were digitized centrally (6). The three best tracings varying by less than 150 ml were averaged to calculate the FEV_1, $FEV_{0.75}$, and FVC, and the tracing with the highest sum of FEV, and FVC was used to calculate the maximal midexpiratory flow (MMEF). All values were corrected to body temperature and pressure saturated with water (BTPS). The child's height and weight were measured in stockinged feet and recorded to the nearest centimeter and pound.

Air Pollution Measurements

A centrally located air monitoring station was established in each community at the time of the first health examination. SO_2, NO_2, O_3, and meteorologic variables were measured continuously. Integrated 24-h TSP samples were collected on a regular schedule. TSP samples were mailed to a central laboratory for determination of total mass concentration. Each site was audited semiannually by an independent agency using National Bureau of Standards traceable reference standards (7).

Beginning in 1978, dichotomous aerosol samplers were installed at each study site (8). The inlet of these samplers removes the larger particles (50% cut-size at 15 µm aerodynamic diameter). The aerosol is then divided into two fractions: the fine fraction with aerodynamic diameter less than 2.5 µm, and the coarse fraction between 2.5 and 15 µm. The two fractions were analyzed for mass concentration by beta-ray attenuation (9) and for elemental concentration by x-ray fluorescence (10). PM_{15} is the sum of the fine and coarse fractions. All elemental sulfur has been assumed to be present as sulfate ion (SO_4). All dichotomous samplers were operational for at least 1 yr prior to the 1980–1981 school year.

Daily mean concentrations of SO_2, NO_2, and O_3 were obtained by averaging hourly concentrations for each day with at least 18 hourly values. Three measures of particle mass ($PM_{2.5}$, PM_{15}, and TSP) were considered, as well as the concentration of elemental sulfate in the fine fraction, denoted here as FSO_4.

Monthly means were calculated for each pollutant by averaging all available daily values. An air pollution exposure in the previous year was calculated for each child by averaging the monthly means for the 12 months preceding the month of the spirometric examination.

Statistical Methods

Previously reported analyses of illness and symptom rates and of pulmonary function levels established that city-to-city variation in health outcomes was larger than would be expected given interindividual variation in health outcomes (1). To account for this variability, we used two-step methods to analyze the health outcomes. In the analysis of illness and symptom rates, an initial logistic regression was used to estimate the adjusted logit of illness frequency in each of the six cities, controlling for sex, age, maternal smoking, and the presence of a gas stove in the home. In the second step, these estimated logits were regressed against the city-specific air pollution measurements using weights that were inversely proportional to the sum of the between-city variance and the within-city variance of the adjusted logits. The results of this regression are summarized here by the estimated relative odds of the illness or symptom rate in the most polluted and least polluted city. Ninety-five percent confidence intervals (95% CI) for these relative odds were calculated using Miettinen's test-based approximation (11).

For the pulmonary function measures, the same general scheme was used. In the first step, the logarithms of individual pulmonary function measurements were fitted to a linear function of the logarithm of height, age, maternal smoking, indicators for sex, parental education, gas cooking, and an interaction between sex and logarithm of height. In the second step, the adjusted city-specific means of the logarithms of pulmonary function measures were regressed on the air pollution variables. Each pollution variable was considered separately. The regression results are summarized by the estimated percentage difference in pulmonary function level between the most polluted and least polluted cities. This difference is given by the antilogarithm of the regression coefficient times the difference in pollutant concentrations. Ninety-five percent confidence intervals were calculated in the logarithmic scale, again using a test-based approximation.

A potentially sensitive subset of the population was defined by the presence of reported asthma or persistent wheeze. The two-step analysis was repeated to produce separate estimates of the air pollution associations in children with and without asthma or wheeze. In the first step, city-specific rates of respiratory symptoms were calculated for each group, after adjusting for the associations with sex, age, parental education, maternal smoking and gas stoves in the combined sample. In the second step, the city-specific adjusted rates were regressed on air pollution, separately for children with and without asthma or wheeze. An analogous procedure was used for analysis of pulmonary function measurements.

Results

A total of 8,131 children were seen during the 1980–1981 school year. Because the enrollment period varied among cities, the age distributions of these children also varied among cities. To avoid confounding caused by age and race, the analysis was restricted to the 5,422 10- to 12-yr-old white children examined in the 1980–1981 school year (table 1).

Adjustment for Covariates

Each symptom was analyzed using a logistic regression model including sex, age, indicators of parental education, maternal smoking (cigarettes per day), an indicator for gas stove, and an indicator for each of the cities. Maternal smoking was significantly associated with most symptoms (table 2). The coefficients for the respiratory symptoms investigated in the earlier report (bronchitis, chronic cough, chest illness, and persistent wheeze) were consistent with values obtained from analysis of the earlier examination (2). Asthma rates were not significantly associated with maternal smoking. Of the referent symptoms, earache was significantly associated with maternal smoking, whereas nonrespiratory illness and hay fever were not. As in the earlier examinations of these children, the presence of a gas stove was not a predictor of current respiratory symptoms. Hay fever was negatively associated with the presence of a gas stove, nonrespiratory illness was positively associated, and no association was found for earache.

The logarithm of pulmonary function was fitted to a multiple linear regression model including sex, sex-specific log of height, age, indicators of parental education, maternal smoking, an indicator for gas stove, and indicators for each city. Maternal smoking was negatively associated with all measures of lung function except FVC (table 3). For FVC and

TABLE 1

CITY-SPECIFIC AGE DISTRIBUTION OF WHITE CHILDREN IN COHORT

	10 yr	11 yr	12 yr	Total
Portage, WI	285	282	245	812
Topeka, KS	252	593	368	1,213
Watertown, MA	240	277	260	777
Kingston, TN	106	198	227	531
St. Louis, MO	283	363	350	996
Steubenville, OH	377	357	359	1,093
Total	1,543	2,070	1,809	5,422

FEV_1, the coefficients were comparable to those reported previously (2). The strongest associations were found for $FEV_{0.75}$ and MMEF, two measures not available in the earlier analysis. Because FVC was positively associated with maternal smoking, the ratios of FEV_1 and MMEF to FVC both had strong negative associations with maternal smoking.

The presence of a gas stove was negatively associated with FVC, FEV_1, and $FEV_{0.75}$. These deficits were not statistically significant, but were comparable to earlier estimates (2). MMEF and the ratio measures were positively associated with gas stove, but the associations were not statistically significant.

The city-specific symptom prevalence and pulmonary function levels, adjusted to the population distribution of the covariates described above, are given in table 4.

Associations with Air Pollutant Concentrations

City-specific annual means of the 24-h average air pollution concentrations were calculated for the 12 months preceding the examination of each child and averaged for each city (table 4). For most pollutants, the annual pollution means were lowest in Portage, Topeka, and Watertown and highest in Kingston, St. Louis, and Steubenville. Ozone concentrations, however, were highest in the communities with low concentrations of other pollutants. Except for ozone, the correlations among pairs of pollution measures varied between 0.53 and 0.98. Ozone concentrations were negatively correlated with all other pollutants, -0.96 with NO_2 and between -0.78 and -0.73 otherwise.

Results from regression of the adjusted logits of symptom frequencies on the air pollutant concentrations, expressed as the relative odds of a positive response in the most- and least-polluted city, are given in table 5. Over the range of TSP concentrations observed (34.1 to 80.0 μg/m³) (table 4), the odds of bronchitis were estimated to increase by a factor of 2.31 with a 95% CI of 0.79 to 6.78, and similar results were obtained for PM_{15} (figure 1), $PM_{2.5}$, and FSO_4, the three other measures of particle mass. The association was statistically significant only for PM_{15}. Smaller and nonsignificant associations with bronchitis rates were found for SO_2 and NO_2. No association was found between ozone concentrations and bronchitis rates. Sex-specific regressions did not indicate any difference in response between the sexes. For example,

TABLE 2

ESTIMATED RELATIVE ODDS (95% CONFIDENCE INTERVAL) OF REPORTED SYMPTOMS VERSUS MATERNAL SMOKING AND GAS STOVES, ADJUSTED FOR SEX, AGE, PARENTAL EDUCATION AND CITY OF RESIDENCE IN CHILDREN 10 TO 12 YEARS OF AGE SIX CITIES STUDY: 1980–1981 SCHOOL YEAR

	Mother's Smoking (1 pack/day)	Gas Stoves
Respiratory symptoms		
Bronchitis	1.28 (1.07; 1.53)	1.02 (0.77; 1.35)
Chronic cough	1.18 (0.98; 1.41)	0.88 (0.67; 1.16)
Chest illness	1.17 (1.01; 1.35)	0.97 (0.79; 1.20)
Persistent wheeze	1.20 (1.04; 1.40)	0.89 (0.71; 1.11)
Asthma	1.07 (0.85; 1.34)	0.76 (0.54; 1.05)
Reference symptoms		
Hay fever	0.92 (0.78; 1.08)	0.70 (0.56; 0.87)
Earache	1.21 (1.09; 1.35)	0.95 (0.81; 1.12)
Nonrespiratory illness	1.16 (0.94; 1.42)	1.30 (0.96; 1.76)

TABLE 3

ESTIMATED PERCENT EFFECT (95% CONFIDENCE INTERVAL) OF MATERNAL SMOKING AND GAS STOVES ON PULMONARY FUNCTION ADJUSTED FOR SEX, SEX-SPECIFIC LOGARITHM OF HEIGHT, AGE, PARENTAL EDUCATION, AND CITY OF RESIDENCE IN CHILDREN 10 TO 12 YEARS OF AGE SIX CITIES STUDY: 1980–1981 SCHOOL YEAR

	Mother's Smoking (1 pack/day)	Gas Stoves
FVC	+0.6% (+0.1, +1.1)	-0.5% (-1.2, +0.2)
FEV_1	-0.4% (-0.9, +0.2)	-0.3% (-1.1, +0.5)
$FEV_{0.75}$	-0.7% (-1.3, -0.2)	-0.2% (-1.0, +0.6)
MMEF	-3.4% (-4.5, -2.4)	+1.0% (-0.5, +2.6)
FEV_1/FVC	-1.0% (-1.3, -0.7)	+0.3% (-0.2, +0.7)
MMEF/FVC	-3.9% (-4.9, -2.9)	+1.5% (+0.0, +3.0)

TABLE 4

CITY-SPECIFIC RATES OF SYMPTOMS, PULMONARY FUNCTION, AND 12-MONTH MEAN POLLUTION CONCENTRATIONS FOR CHILDREN 10 TO 12 YEARS OF AGE SIX CITIES STUDY: 1980–1981 SCHOOL YEAR

	Portage	Topeka	Watertown	Kingston	St Louis	Steubenville
Respiratory symptoms, %						
Bronchitis	3.6	6.0	4.7	10.0	6.4	8.1
Chronic cough	3.0	7.3	2.3	6.7	6.6	8.7
Chest illness	7.6	11.7	9.3	15.9	7.2	16.1
Persistent wheeze	9.6	11.4	6.6	10.6	8.9	9.6
Asthma	5.1	5.9	3.2	4.4	3.4	3.3
Reference symptoms, %						
Hay fever	20.0	22.7	12.1	23.1	32.8	23.1
Earache	10.7	12.6	10.9	6.7	12.7	5.7
Nonrespiratory illness	4.9	4.3	6.0	5.1	4.5	4.5
Pulmonary function, L						
FVC	2.556	2.492	2.511	2.487	2.511	2.539
FEV_1	2.225	2.142	2.178	2.156	2.166	2.191
$FEV_{0.75}$	2.042	1.960	2.002	1.988	1.983	2.007
MMEF	2.635	2.529	2.585	2.607	2.589	2.611
Pulmonary function ratios						
FEV_1/FVC	0.870	0.859	0.867	0.868	0.862	0.863
MMEF/FVC	1.030	1.014	1.030	1.047	1.031	1.030
Particulate pollution, μg/m³						
TSP	34.1	63.2	53.8	63.8	80.0	71.2
PM_{15}	20.1	33.4	25.8	42.3	37.8	58.8
$PM_{2.5}$	12.7	11.8	17.7	25.7	22.0	36.7
FSO_4	4.3	3.2	5.7	7.9	7.1	13.9
Gaseous pollution, ppb						
SO_2	4.2	3.5	10.5	6.5	13.5	27.8
NO_2	6.5	12.7	19.9	15.4	22.6	22.6
O_3	37.8	30.3	22.0	25.4	23.2	18.0

Definition of abbreviations: TSP = total suspended particles; PM_{15} and $PM_{2.5}$ = particulate matter less than 15 μm and 2.5 μm aerodynamic diameter; FSO_4 = fine-fraction aerosol sulfate.

TABLE 5

ESTIMATED RELATIVE ODDS OF SYMPTOMS AND 95% CONFIDENCE INTERVAL BETWEEN THE
MOST POLLUTED AND LEAST POLLUTED CITIES FOE EACH POLLUTANT UNIVARIATELY

	TSP	PM_{15}	$PM_{2.5}$	FSO_4	SO_2	NO_2	O_3
Respiratory symptoms							
Bronchitis	2.3 (0.8, 6.8)	2.5 (1.1, 6.1)	2.1 (0.8, 5.9)	2.0 (0.6, 6.7)	1.5 (0.4, 5.8)	1.7 (0.5, 5.5)	0.5 (0.2, 1.7)
Chronic cough	3.4 (0.7, 14.5)	3.7 (1.0, 13.5)	2.3 (0.4, 13.2)	2.2 (0.3, 15.2)	1.8 (0.3, 12.5)	1.6 (0.3, 10.5)	0.6 (0.1, 4.5)
Chest illness	1.4 (0.3, 6.5)	2.3 (0.8, 6.7)	2.0 (0.6, 6.2)	1.9 (0.5, 6.9)	1.5 (0.4, 5.9)	1.2 (0.3, 4.8)	0.6 (0.2, 2.5)
Persistent wheeze	1.1 (0.5, 2.5)	1.2 (0.5, 2.6)	1.0 (0.5, 2.2)	1.0 (0.4, 2.2)	0.9 (0.4, 1.9)	0.8 (0.4, 1.6)	1.2 (0.6, 2.7)
Asthma	0.7 (0.3, 1.9)	0.7 (0.3, 2.0)	0.6 (0.3, 1.4)	0.6 (0.3, 1.4)	0.6 (0.3, 1.2)	0.6 (0.3, 0.9)	1.9 (1.0, 3.4)
Reference symptoms							
Hay fever	0.9 (0.2, 3.8)	0.5 (0.2, 1.2)	0.4 (0.2, 0.9)	0.4 (0.2, 0.9)	0.6 (0.2, 1.7)	0.8 (0.2, 2.8)	1.6 (0.4, 6.0)
Earache	2.1 (0.6, 7.4)	1.6 (0.4, 7.0)	1.3 (0.3, 5.6)	1.3 (0.3, 6.0)	1.2 (0.3, 5.3)	1.2 (0.3, 4.9)	1.0 (0.2, 4.7)
Nonrespiratory illness	0.9 (0.5, 1.4)	0.9 (0.6, 1.4)	1.0 (0.6, 1.6)	1.0 (0.6, 1.6)	1.0 (0.6, 1.5)	1.0 (0.6, 1.6)	0.9 (0.6, 1.6)

For definition of abbreviations, see table 4.

the estimated odds for bronchitis versus PM_{15} was 2.48 for boys and 2.60 for girls. Similar associations were found for chronic cough and chest illnesses. The odds of reported illness were estimated to increase by approximately a factor of two across the range of particulate exposures. Much weaker positive associations were found with SO_2 and NO_2, and a negative association with ozone.

Persistent wheeze was not associated with any of the air pollution measures. Asthma rates were negatively associated with all pollutants except ozone. A similar pattern was found for hay fever, suggesting a higher reporting among those children in the more rural communities. Asthma and hay fever rates were positively associated with annual mean ozone concentrations—estimated relative odds for asthma, 1.88 (95% CI, 1.03 to 3.43) and for hay fever, 1.62 (95% CI, 0.44 to 6.0). Of the other two reference symptoms considered, earache had a weak positive association with the particulate measures, and nonrespiratory illness had estimated relative odds very close to one for each pollutant.

Only TSP concentration was consistently associated with estimated lower levels of pulmonary function. Over the range of concentrations observed, the largest deficit, -2.7% (95% CI, -6.5 to $+1.2\%$), was found for $FEV_{0.75}$. There was little evidence for an association between lower pulmonary function level and the annual mean concentration of any other pollutant.

Susceptible Populations

The prevalence of respiratory symptoms was much higher among the 571 children with asthma or persistent wheeze than among children without these symptoms. Bronchitis was reported among 25.5% of the children with asthma or wheeze versus 4.0% among those without; for chronic cough the rates were 29.5% versus 3.2%, and for chest illness 36.5% versus 7.6%. Although FVC was only 0.3% lower among these children with asthma
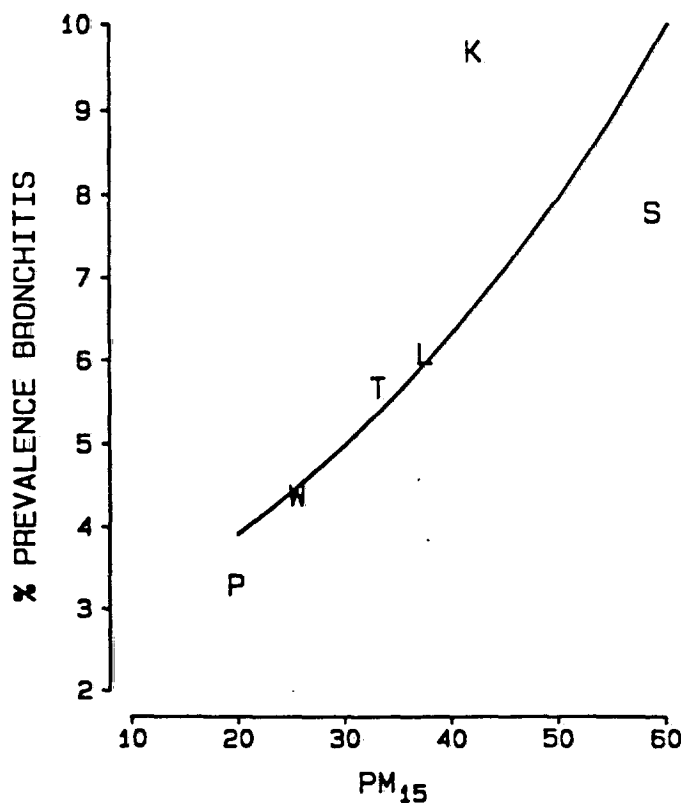

Fig. 1. City-specific prevalence of reported bronchitis versus annual mean PM_{15} concentrations $(\mu g/m^3)$ and logistic fit to data (P = Portage, T = Topeka, W = Watertown, K = Kingston, L = St Louis, and S = Steubenville).

TABLE 6

ESTIMATED RELATIVE ODDS OF RESPIRATORY SYMPTOMS AND 95% CONFIDENCE INTERVAL BETWEEN THE MOST POLLUTED AND LEAST POLLUTED CITY FOR EACH POLLUTANT UNIVARIATELY, STRATIFIED BY REPORTED ASTHMA OR PERSISTENT WHEEZE

	Wheeze or Asthma	TSP	PM_{15}	$PM_{2.5}$	FSO_4	SO_2
Bronchitis	No	2.0	2.2	1.8	1.7	1.5
		(0.9, 4.7)	(1.1, 4.2)	(0.8, 4.3)	(0.6, 4.7)	(0.5, 4.3)
	Yes	3.2	3.8	3.5	3.1	2.0
		(0.6, 18.1)	(0.9, 15.5)	(0.9, 13.2)	(0.6, 16.8)	(0.3, 14.3)
Chronic cough	No	4.1	4.1	3.0	2.9	2.4
		(1.6, 10.3)	(1.9, 9.2)	(0.9, 10.7)	(0.6, 13.1)	(0.5, 11.7)
	Yes	4.0	5.0	2.4	2.4	1.9
		(0.2, 78.2)	(0.4, 71.6)	(0.1, 49.5)	(0.1, 60.6)	(0.1, 44.1)
Chest illness	No	1.2	2.1	1.9	1.9	1.5
		(0.3, 5.4)	(0.7, 6.4)	(0.6, 5.7)	(0.6, 6.4)	(0.4, 5.6)
	Yes	2.3	3.8	3.1	2.9	1.9
		(0.3, 16.7)	(1.1, 13.5)	(0.7, 12.8)	(0.5, 15.6)	(0.3, 13.0)

For definition of abbreviations, see table 4.

or wheeze, FEV₁ was 4.5% lower, $FEV_{0.75}$ was 4.3% lower, and MMEF was 10.6% lower. These children were considered as a potentially susceptible subgroup, and the associations between air pollutant concentrations and adjusted city-specific respiratory symptom rates and pulmonary function levels for children with and without these symptoms were compared.

The estimated relative odds over the range of each of the particulate measures and SO_2 is given separately for the two groups in table 6. Bronchitis rates gave relative odds of 2.2 (95% CI, 1.1 to 4.2) versus PM_{15} for children without asthma or wheeze. The estimated relative odds were higher, 3.8 (95% CI, 0.9 to 15.5), for those reporting asthma or wheeze. Children reporting asthma or wheeze not only had a higher prevalence of bronchitis, but apparently a stronger association with PM_{15} concentrations (relative odds ratio, 3.8/2.2 = 1.7; 95% CI, 0.5 to 6.3). Although this difference is not statistically significant on the logistic scale, when these results are plotted on a linear prevalence scale (figure 2), it is clear that children with asthma or wheeze were reporting most of the excess number of cases of bronchitis in the more polluted communities. Similar associations were found between bronchitis and each of the other particulate measures. The associations of bronchitis with SO_2 were smaller in magnitude than with the particulate measures, but were larger for children with asthma or wheeze than for those without (table 6). Results for chest illness in the past year were comparable to those for bronchitis, except that the SO_2 association was smaller among children with asthma or wheeze. The association between pollutant concentration and chronic cough was not stronger, however, among those with asthma or wheeze (table 6).

Separate regressions of the adjusted city-specific pulmonary function levels on air pollution for children with and without asthma or wheeze did not show any associations (figure 3).

Discussion

The first aim of these analyses was to re-examine the previously reported associations between air pollution concentrations and respiratory illness and symptom rates in the same children an average of 3 yr older, using exposure data of documented quality obtained under a standardized protocol. These reanalyses showed associations of particulate and sulfur oxide concentrations with respiratory illness and symptom rates that correspond closely to those found in the earlier analyses. Thus, these findings cannot be attributed to errors in the measurement of ambient air pollution concentrations.

In the earlier analyses (1), annual mean TSP concentrations varied between 39.3 µg/m³ in Portage and 114.1 µg/m³ in Steubenville. This range was associated
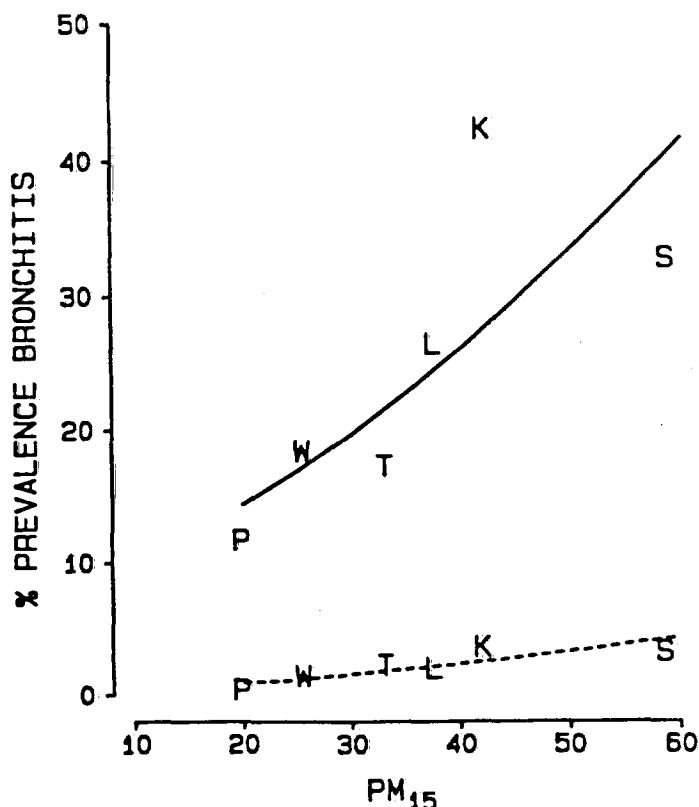

Fig. 2. City-specific prevalence of reported bronchitis versus annual mean PM_{15} concentrations (µg/m³) stratified by reported asthma or persistent wheeze. Upper curve (solid line) is the logistic fit for children with reported asthma or wheeze, and lower curve (dashed line) is the logistic fit for those without (see figure 1 for city labels).
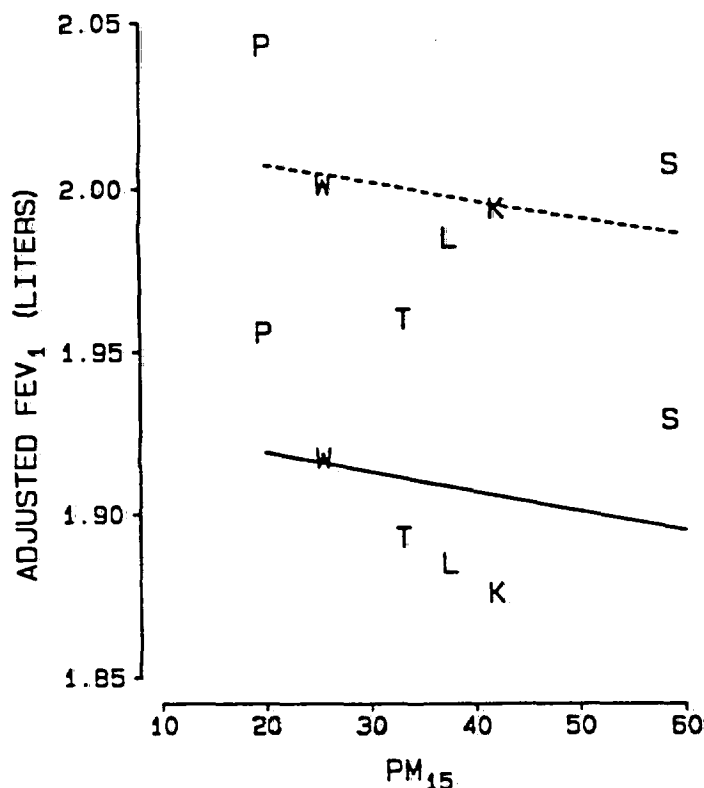
Fig 3. City-specific adjusted FEV, versus annual mean PM_{15} concentrations ($\mu g/m^3$) stratified by reported asthma or persistent wheeze. Lower curve (solid line) is the linear fit for children with reported asthma or wheeze, and upper curve (dashed line) is for those without (see figure 1 for city labels).

with a between-cities relative odds for chronic cough of 2.13 with a 95% CI of 1.63 to 2.77. Similarly, the relative odds were 2.13 (95% CI, 1.08 to 4.18) for bronchitis, 1.34 (95% CI, 0.70 to 2.55) for chest illness, and 1.23 (95% CI, 0.76 to 7.00) for persistent wheeze. Despite a decline in the TSP concentrations in the most polluted cities, Steubenville and St. Louis, between the first two examinations in the 1975 to 1977 school years and the 1980–1981 school year, the estimated relative odds obtained in the current analysis are comparable to those obtained earlier. The estimated relative odds for the referent symptoms of hay fever and nonrespiratory illness were not elevated. A positive association was found between earache and particulate pollution, although the association was far from statistical significance. This is consistent with the increased prevalence of earache associated with maternal smoking (table 2).

The differences in respiratory illness reporting between cities may represent differences in the samples of children that are unrelated to air pollution exposure.

Those cities visited in the spring have been noted to have both higher rates of respiratory symptom reporting and higher air pollution values. Hence, the positive associations may be attributable in part to better recall of symptoms in the previous winter when questionnaires were administered in the spring compared with those administered in the fall. When season of examination was included in the regression analyses, the estimated relative odds of symptom reporting were reduced. For example, the estimated effect of PM_{15} on reported bronchitis was reduced from 2.52 (table 5) to 1.97 when adjusted for season. Other potential confounders include differences in interpretation of the questionnaire by the respondent and persistent differences in illness or reporting rates associated with ethnic or cultural factors.

The city-specific symptom reporting rates and adjusted level of pulmonary function have been shown to be consistent within each city year to year (1). However, the variability of these summary measures between cities was larger

then the random fluctuation between individuals would predict. Because of this clustering effect in the data, two-step methods were used to analyze the health outcomes. The effect of these methods is to produce conservative estimates of the statistical significance of the reported associations compared with commonly used methods. For example, if bronchitis were regressed on PM_{15} exposure for each child, adjusting for covariates in a logistic model, a highly significant positive association is found (p = 0.000024). Using the two-step method, bronchitis had a marginally significant positive association with PM_{15} (p = 0.016). The estimated odds ratios are similar in both cases. The confidence intervals presented here reflect this adjustment for the clustering of response within city.

In the previous report, data from 3 yr were considered in each city, and three of the cities (Kingston-Harriman, St. Louis, and Steubenville) were divided into two exposure regions based on topography, local sources of pollutants, and air pollution measurements from multiple monitors. This permitted evaluation of the covariance of health status and air pollution within cities. By 1980, there was no evidence for spatial differences in exposure within Kingston-Harriman or St. Louis. The air monitor in Steubenville was located centrally, at a location intermediate between the two previously defined air pollution regions. Thus, the data from the 1980–1981 school year did not allow investigation of the spatial or temporal covariation of air pollution and respiratory health within cities.

The second aim was to investigate the effects of pollutants other than TSP, SO_2, and SO_4, particularly measures of fine particulate air pollution. Because data were available for only six cities, however, the information differentiating pollutants is somewhat limited. Each pollutant was therefore considered univariately, and multivariate comparisons were not attempted.

All of the particulate measures, TSP, PM_{15}, $PM_{2.5}$, and FSO_4, are highly correlated across the six cities. All are associated with substantial increases in the reported rates of respiratory illnesses over the range of annual means observed. Each of these particulate measures has well-known limitations (12, 13). TSP has a poorly defined upper size cut that depends on wind speed and direction. PM_{15} may underestimate exposure because of coarse particle loss in shipping (14). $PM_{2.5}$ is lightly contaminated by less than absolute separation of particles at 2.5 μm.

The FSO_4 concentration may overestimate sulfur concentrations slightly because of conversion of SO_2 to SO_4 on the filter and the assumption that all sulfur is SO_4.

Of the particulate measurements, only associations with PM_{15} were statistically significant. Dzubay and Barbour (14) have reported a loss of between 19 and 53% of coarse particle mass from filters during shipping between the sample site and the laboratory. The potential variable loss of coarse particles in shipping and handling would normally cause concern about the validity of the associations with PM_{15}. However, starting late in 1980, independent measurements of PM_{15} were made by high-volume samplers with sampling heads that removed particles with an aerodynamic diameter greater than 15 μm. The annual mean concentrations for 1981 from these samplers were 22.8 μg/m³ in Portage, 37.6 μg/m³ in Topeka, 29.8 μg/m³ in Watertown, 41.5 μg/m³ in Kingston, 44.3 μg/m³ in St. Louis, and 62.6 μg/m³ in Steubenville. Comparison with PM_{15} concentrations (table 4) shows that the inhalable particulates were higher by an average of 3.4 μg/m³ and the correlation between the annual means was 0.98. Thus, any bias in the PM_{15} caused by shipping losses in these samples must be small. Moreover, such randomly variable error in the exposure measurement would only underestimate the true association.

Bronchitis and chest illness rates were noted to be higher in Kingston than in any of the other cities, including Steubenville, which has the highest particulate pollution concentrations. Lippmann (15) has suggested that these higher respiratory illness rates may be due to the acidity of the suspended particles in Kingston and Steubenville. Acidity measurements were not made in 1980 or 1981, but recent measurements have shown that aerosol acidity is in fact higher in Kingston and Steubenville (16).

Sulfur dioxide, which is also correlated with the particulate measures, has a much weaker association with the respiratory symptoms than the particulate measures. Similar results were found in the earlier study. Nitrogen dioxide annual means are higher in the more urbanized cities (Watertown and St. Louis) and the industrial city (Steubenville) than in the more rural cities (Portage, Topeka, and Kingston). The association of NO_2 with respiratory symptoms, however, was weak.

Ozone concentrations were highest in the most rural community (Portage).

Ozone is a secondary pollutant formed by photochemical reactions as polluted air masses move away from the pollution source regions. Primary pollutants such as nitric oxide (NO) rapidly scavenge O_3, converting it to molecular oxygen and the NO to NO_2. Thus, ozone levels tend to be low in regions that are sources of these primary pollutants such as Steubenville, St. Louis, and Watertown and high in more pristine areas such as Portage, Topeka, and Kingston. Negative associations of respiratory symptoms with ozone probably do not represent a protective effect of ozone, but rather indicate the negative correlation between ozone and other pollutants.

The third aim was to test for associations between air pollution and tests of pulmonary function potentially more sensitive than the previously reported FVC and FEV_1. Although $FEV_{0.75}$ and MMEF were more strongly associated with maternal smoking than were FVC or FEV_1, there was still no indication of chronic effects of air pollution on any measure. Lippmann and Lioy (12) has suggested that these chronic effects may be masked by acute changes in pulmonary function associated with exposure on the days or hours immediately before the examination. The annual pulmonary function data are being analyzed to evaluate such acute effects, and will be reported separately.

The analyses were repeated with stratification on reported asthma or persistent wheeze. Although children with reported asthma or persistent wheeze made up only about 10% of the sample, they accounted for approximately half of the children reporting chronic respiratory symptoms. Thus, stratifying by reported asthma or wheeze removes a substantial source of variability in illness and symptom responses. The separate regressions permit comparisons of the air pollution associations in the two groups of children. Positive associations were found between bronchitis, chronic cough, and chest illness and the particulate measures for both groups. The estimated relative odds of bronchitis and chest illness for the particulate measures was approximately twice as large for those with asthma or wheeze, although these differences were not statistically significant. In absolute terms, the adjusted bronchitis rate for children without asthma or wheeze increased from 2.4% in Portage to 5.2% in Steubenville, a rate difference of 2.8% (see figure 2). For children with asthma or wheeze, the adjusted bronchitis rate increased from 13.7%

in Portage to 34.7% in Steubenville, a rate difference of 21.0%. Thus, the smaller group of children that reported asthma or wheeze contributes to most of the cases of bronchitis that could be attributed to air pollution.

In summary, these analyses provide further evidence that there is an increase in respiratory symptom reporting across the six cities that is associated with annual mean particulate levels in these communities. Stronger associations were found with concentrations of inhalable particles, PM_{15}, although the power to differentiate the effects of specific size ranges was weak. Unexplained differences in symptom reporting between cities may be explained by specific components of the particle exposure not considered, e.g., aerosol acidity. Such associations are being investigated in later follow-up examinations of these and other cohorts of children.

Children with reported persistent wheeze or asthma were found to have substantially higher reporting rates for respiratory illnesses and lower pulmonary functions. The proportion of these children within the sample varies between communities. In the more polluted communities, a large fraction of these children are reporting respiratory symptoms. Thus, these children appear to be reacting more in response to air pollution exposure than the rest of the sample. Controlled exposure studies of adolescent asthmatics (17) have suggested that such children may be especially responsive.

There was no evidence for an effect of pollution exposure on level of pulmonary function, either in the complete cohort or in the children with reported persistent wheeze. Thus, air pollution exposure may increase respiratory symptom rates without causing irreversible pulmonary function losses. Nevertheless, although respiratory symptoms may be transient, they clearly have health consequences of some importance. In particular, respiratory illness in childhood has been reported as a risk factor for the subsequent development of respiratory diseases in adulthood and also a risk factor for the development of COPD in smokers (18). Longitudinal analysis of data provided by these children as they pass through adolescence may provide additional information about the long-term effects of these pollutant exposures.

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Ownby, D.R., McCullough, J. "Passive exposure to cigarette smoke does not increase allergic sensitization in children" Journal Allergy Clin Immunol 82: 634-637, 1988.

SUMMARY: The purpose of this study was to learn whether children passively exposed to parental cigarette smoke would be more frequently sensitized to common allergens or would have higher concentrations of allergen-specific IgE. To evaluate this question, we studied tow groups of children aged 2 to 17 years. The first group consisted to 100 children selected from a general pediatric group practice. These children were being observed for well-child care, and the only selection criteria were the need for a venous blood sample for a reason unrelated to the study. The second group of 91 patients were consecutively referred from the same pediatric group for allergy evaluation because of respiratory tract symptoms. Parental smoking histories were obtained, and total serum IgE, IgD, and IgE specific for cat, dog, mite, ragweed, grass, and cockroach were measured by ELISA. Children of smoking mothers had significantly greater IgD concentrations ($p = 0.03$) and were more likely to be referred for allergy evaluation ($p = 0.0001$), but these children did not have increased concentrations of total or allergen-specific IgE. Exposed children were not more likely to be serologically sensitive to any of the allergens tested. We conclude that children passively exposed to cigarette smoke do not produce more IgE to common allergens nor are they more likely to produce IgE to any particular allergen.

Passive exposure to cigarette smoke does not increase allergic sensitization in children

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The purpose of this study was to learn whether children passively exposed to parental cigarette smoke would be more frequently sensitized to common allergens or would have higher concentrations of allergen-specific IgE. To evaluate this question, we studied two groups of children aged 2 to 17 years. The first group consisted of 100 children selected from a general pediatric group practice. These children were being observed for well-child care, and the only selection criteria were the need for a venous blood sample for a reason unrelated to the study. The second group of 91 patients were consecutively referred from the same pediatric group, for allergy evaluation because of respiratory tract symptoms. Parental smoking histories were obtained, and total serum IgE, IgD, and IgE specific for cat, dog, mite, ragweed, grass, and cockroach were measured by ELISA. Children of smoking mothers had significantly greater IgD concentrations (p = 0.03) and were more likely to be referred for allergy evaluation (p = 0.0001) but these children did not have increased concentrations of total or allergen-specific IgE. Exposed children were not more likely to be serologically sensitive to any of the allergens tested. We conclude that children passively exposed to cigarette smoke do not produce more IgE to common allergens nor are they more likely to produce IgE to any particular allergen. (J ALLERGY CLIN IMMUNOL 1988;82:634-7.)

A number of studies have suggested that exposure to cigarette smoke may increase the risk of allergic sensitization in children,[1-9] but direct evidence of such an effect has been very limited. Children exposed to cigarette smoke, as the result of smoking mothers, have an increased frequency of respiratory illness.[1-6] Kjellman[7] found that children with atopic family histories had significantly higher total IgE concentrations, at 9 and 36 months of age, if their parents smoked. Weiss et al.[8] found that the prevalence of at least one positive skin test to a group of four common allergens was nearly doubled if the child's mother smoked. A study in rats also demonstrated that cigarette-smoke exposure increased serum IgE levels and enhanced specific IgE formation apparently by a local effect on the airways.[9]

The purpose of this study was to learn whether children exposed to parental cigarette smoke would

Abbreviation used	
ANOVA:	Analysis of variance

have a higher frequency of serologic sensitivity to common allergens or increased concentrations of allergen-specific IgE. Two cohorts of children were examined: a cohort of 100 children being observed for well-child care, and a cohort of 91 children with respiratory symptoms who were referred for allergy evaluation. We did not find any significant relationships between either maternal or paternal cigarette smoking and IgE in the 191 children studied.

PATIENTS AND METHODS

The study protocol was approved by the Henry Ford Hospital Human Rights Committee. Written informed consent was obtained from parents, and assent was obtained for children older than 12 years. The subjects were younger than 17 years of age and were recruited from two populations. The pediatric cohort was recruited from children aged 1 to 17 years who were being observed by a group of pediatricians for well-child care (e.g., immunizations, preschool, and camp or athletic physicals). If a blood sample was to be obtained for a purpose unrelated to this study, the parent and child were asked to participate in this study. As much as possible, consecutive patients meeting these criteria

were enrolled. After consent was obtained, a questionnaire concerning family smoking habits was completed by a nurse, and a blood sample for IgE measurement was obtained. The questionnaire covered estimates of the smoking of both parents and any other regular member of the household in terms of packages of cigarettes smoked per day, rounded to the nearest one-half pack, and also if the parents had smoked since the child was born or if they had started smoking afterward. Children older than the age of 10 years were questioned about personal smoking away from their parents, and if they stated that they smoked regularly or if they had ever smoked more than 10 cigarettes, they were excluded from the study.

The allergy cohort consisted of consecutive patients referred by the same group of pediatricians for allergy evaluation. These children were referred for evaluation of chronic or recurrent respiratory symptoms, including rhinitis, asthma, chronic serous otitis media, or a combination of symptoms. They were evaluated for allergy as clinically indicated, and the same questionnaire concerning family smoking status was completed. If a child had been previously enrolled as part of the pediatric cohort before referral to allergy was contemplated, they remained in the pediatric cohort. No patient was included in both the allergy and pediatric cohorts.

Both the pediatric and allergy cohorts were predominantly from a middle to upper middle-class community. Selection for either cohort was not based on parental smoking, socioeconomic status, sex, or race. Children in the pediatric cohort were expected to be somewhat older, since many were being observed for preschool, precamp, or preathletic examinations.

IgE and IgD measurements

Both total serum and allergen-specific IgE measurements were performed with ELISA, as previously described.[10] The allergens studied were cat, dog, house dust mite (Dermatophagoides farinae), cockroach, timothy grass, and short ragweed. Briefly, allergen-specific IgE was measured by absorbing the relevant allergen to plastic microtiter strips (MicroFLUOR Removawell, Dynatech, Inc., Alexandria, Va.), which were then washed and blocked to prevent further passive absorption. Fifty microliter aliquots of patient serum were then added to duplicate wells and incubated overnight. After washing, biotinated, immunospecifically purified antihuman IgE (Kirkegaard-Perry Laboratories, Gaithersburg, Md.) was added to the wells, followed by another incubation and wash cycle. Avidin-alkaline phosphatase conjugate (Sigma Chemical Co., St. Louis, Mo.) was then added, followed by a wash, and finally the addition of 4-methylumbelliferyl phosphate. The fluorescence of the product of the enzyme reaction was read in a microfluorometer (MicroFLUOR). The fluorescence is proportional to the amount of specific IgE in the patient's sample. A pool of sera lacking IgE specific for the study allergens but having a total IgE concentration of 325 IU/ml of IgE was assayed in quadruplicate for each allergen in each assay run. Results of patient samples are expressed as multiples above

TABLE I. Characteristics of study population

	Pediatric cohort	Allergy cohort	p Values
No.	100	91	
Mean age range (1-17 yr)	9.2	7.1	0.0003
M:F	35:65	46:45	0.03
% Maternal smoking	25	52	0.0001
% Paternal smoking	32	45	0.06
Mean IgE (IU)	84	62	0.36
Mean IgD (IU)	10.3	14.1	0.12
% Serologic atopy	58	67	0.20

this negative control pool. A value of two or more, which equals the mean plus 4 SD, is considered definitely positive for allergen-specific IgE. Positive controls were also included in each assay run.

Total serum IgE was determined as previously reported.[10] The assay was similar to the ELISA used for specific IgE except that the wells were first coated with purified antihuman IgE (Kirkegaard-Perry Laboratories). Appropriate dilutions of the patient sera were added to triplicate sets of wells. After washing, the remaining steps are the same as for specific IgE determinations. The values of unknown samples in units were determined from a standard curve constructed from appropriate dilutions of a serum pool that had been standardized against the U.S. reference standard.

Serum concentrations of IgD were determined with the same type of ELISA system as that used for IgE, except that antihuman IgD (Tago Inc., Burlingame, Calif.) was substituted for the anti-IgE. The standard serum pool used to construct the standard curve was standardized against the World Health Organization IgD reference No. 67137. Results for both total IgE and IgD are in international units.

Statistical analysis

These data were analyzed by the Michigan Interactive Data Analysis System with the statistical tests, as stated in the text.[11] For comparison of group means, the parametric Student's t test was computed. When the Student's t test was invalid because of different group variances or nonnormal distributions, the nonparametric Mann-Whitney test was used. Total serum IgE concentrations were converted to logarithmic equivalents to normalize the distributions before analysis. Two children in the allergy cohort whose parents stated that they smoked regularly, but smoked five or fewer cigarettes per day, were excluded from analysis. There were no cases in which a family member regularly smoked something other than cigarettes. For the purpose of grouping patients by maternal or paternal smoking, a history of one-half pack per day or more was considered smoking. The significance of differences between proportions of groups was computed by the chi-square statistic. To learn whether there was a relationship between the quantity of parental smoking and IgE formation, ANOVA was used.

TABLE II. Total allergen-specific IgE* and total IgD* by maternal smoking status

	Maternal smoking		
	No	**Yes**	**p Values**
IgE (IU)	55.9*	43.0*	0.28
IgD (IU)	10.3*	15.3*	0.03
Cat	2.8*	3.1*	0.37
Dog	2.6	3.4	0.62
Mite	1.8	1.9	0.36
Ragweed	2.8	2.5	0.34
Timothy	3.5	3.7	0.28
Cockroach	2.0	1.8	0.90

*Total IgE and IgD values are the geometric means in international units. Specific IgE values are the mean multiples above a negative control pool.

For ANOVA the data for maternal and paternal smoking was grouped into four categories: nonsmoking, 0.5 pack per day, 1.0 to 1.5 packs per day, and two or more packs per day.

RESULTS

The characteristics of the study population are presented in Table I. One hundred ninety-one children ranging from 1 to 17 years of age were admitted to the study. The 100 children in the pediatric cohort were somewhat older and had a greater proportion of female children. The most significant difference between the two cohorts was a 25% frequency of maternal smoking in the pediatric cohort compared to a 52% frequency of maternal smoking in the allergy cohort ($p = 0.0001$).

There were no reports of either the mother or father having started smoking after the child was more than 1 month of age; therefore, all children were exposed throughout their entire life. Some mothers had stopped smoking during pregnancy but restarted soon after delivery.

Since previous studies have demonstrated that maternal smoking is more likely to be related to child health problems, the initial data analysis concentrated on this variable. The results of comparing the total serum concentrations of IgE and IgD, and the relative serum concentrations of allergen-specific IgE, based on maternal smoking status, are presented in Table II. When the total study population is considered, neither the total nor the allergen-specific IgE concentrations differed significantly between exposed and nonexposed children. The mean IgD concentration was significantly higher in the children of smoking mothers.

In the pediatric cohort, no significant differences

TABLE III. Frequency of serologic sensitization to each allergen

	Maternal smoking		
Allergen	**No (%)**	**Yes (%)**	**p Values**
Cat	41.0	45.8	0.53
Dog	33.6	30.6	0.66
Mite	19.3	19.4	0.98
Ragweed	31.1	27.8	0.63
Timothy	18.5	19.4	0.87
Cockroach	13.8	17.6	0.48

were found for any of the immunologic variables between exposed and nonexposed children. In this cohort the mean serum-IgD concentration was not significantly elevated in exposed children. Similarly, no significant differences in any of the mean IgE values were found in the allergy cohort, but IgD was significantly elevated in exposed children (11.3 versus 17.2 IU; $p = 0.01$).

We believe the failure to find differences between exposed and nonexposed children could be due to the fact that cigarette smoke might only affect children genetically predisposed to produce specific IgE. We therefore defined a group of children as serologically atopic based on at least one positive in vitro test for allergen-specific IgE. As expected, there was a general increase in all of the IgE values, but there were no significant differences between the exposed and nonexposed children. The significantly increased mean IgD was again found in the children of smoking mothers (10.4 versus 17.2 IU; $p = 0.01$).

Another possible explanation for our failure to find a significant difference between groups may be because of age-induced variation in the antibody measurements. As expected, both total IgE and IgD concentrations were significantly correlated with age (Ln IGE versus age: $r = 0.23$ and $p = 0.0012$; and Ln IgD versus age: $r = 0.20$ and $p = 0.0096$). The results of correlating age with the logarithms of allergen-specific IgE concentrations were variable: cat, $r = 0.01$ and $p = 0.92$; dog, $r = 0.03$ and $p = 0.66$; mite, $r = 0.15$ and $p = 0.04$; ragweed, $r = 0.20$ and $p = 0.0068$; timothy, $r = 0.09$ and $p = 0.20$; and cockroach, $r = 0.12$ and $p = 0.11$. We therefore used analysis of covariance to learn whether controlling for the effect of age would allow us to detect significant differences between exposed and nonexposed children that were not observed in the original analysis. The differences between chil-

dren exposed and not exposed to maternal cigarette smoke remained insignificant for all of the IgE variables, even after controlling for the effect of age.

We repeated all of the analysis presented in Table II separately for male and female children and found no significant differences for any IgE variable. We also repeated all the same comparisons found in Table II with both paternal smoking or smoking by either parent and found no significant differences for any IgE variable.

We next considered that exposure to maternal smoking might not increase allergen-specific IgE production, but it might increase the risk of sensitization (production of a detectable amount of IgE to one or more allergens). We therefore analyzed the data of the total group of children for the frequency of a positive in vitro test for each allergen. The results are presented in Table III. There are no significant differences in the frequency of sensitization between the children based on maternal smoking. We again repeated the analysis with only those children with at least one positive specific IgE test, and there were no significant differences in the frequency of sensitization to any of the allergens studied.

We also observed both the quantities of IgE to common allergens and the frequency of sensitization in children based on the quantity of smoking reported by the mother with ANOVA and found no significant differences. Similarly, the quantity of paternal smoking was not related to IgE (data not presented).

DISCUSSION

Previous studies have consistently demonstrated that children exposed to parental smoking have higher frequencies of respiratory illness.[1-6] Maternal smoking is usually more closely related to the increase in symptoms than is paternal smoking.[1-6] Since others have reported higher rates of allergic sensitization to occupational allergens in smoking workers[12, 13] and since animal experiments suggest that cigarette-smoke exposure can increase the rate of sensitization to allergens,[9] we believe that the increase in respiratory disease in children exposed to cigarette smoke might be the result of increased allergic sensitization.

The purpose of this study was therefore to determine if parental cigarette smoking was related to the presence or quantity of total and allergen-specific IgE in children. In the two cohorts of children studied, we did not find any evidence relating IgE to cigarette-smoke exposure. This study does not suggest that cigarette-smoke exposure is innocuous for children. The fact that the mothers of twice as many children in the allergy cohort smoked compared to the pediatric

cohort suggests that maternal smoking produced sufficient respiratory symptoms in some children to prompt an allergy referral. This observation is consistent with the previously mentioned studies demonstrating increased respiratory symptoms in exposed children. We did not attempt to relate cigarette smoke exposure to the symptoms of allergic disease, merely to the presence and quantity of IgE antibodies.

The failure of our data to refute our null hypothesis that passive cigarette-smoke exposure does not affect IgE production suggests either the null hypothesis is true or that we failed to study an adequate number of children. We therefore calculated the power of the study or the probability that if a true difference existed we would have detected it, given the current sample size. If we consider the entire sample of 191 and the concentrations of cat-specific IgE, and if we assume that the geometric mean cat IgE concentration would need to double to be clinically significant, the power of this study is 0.97, or there is a 97% probability that this study would have detected a doubling of cat-specific IgE at the 0.05 significance level. The power for dog was 0.99; ragweed, 0.99; and total IgE, 0.999, given the same assumptions. We believe that requiring a doubling of the mean IgE concentrations is modest because in a previous study relating grass-specific IgE to symptoms, we found threefold to fivefold increases in the geometric mean allergen-specific IgE concentrations between different symptomatic groups.[10]

A possible problem with our study is our reliance on self-reporting of smoking by the parent accompanying the child, usually the mother. Other investigators have reported strong correlations between reported maternal smoking and objective measures of cigarette-smoke absorption, such as urinary or serum cotinine concentrations.[14, 15] Additional data in this study, supporting the proper classification of the children, are the significant increase in IgD in the children exposed to maternal smoking. Other investigators have reported increased concentrations of IgD in adult smokers[16] and increased cord blood IgD in children born to smoking parents.[17]

In summary, we did not find any evidence to suggest that the increased respiratory disease found in children exposed to smoking mothers is related to IgE production, but our data do suggest that maternal cigarette smoking results in increased respiratory symptoms in children.

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Evaluation of a radioimmunoassay for histamine measurement in biologic fluids

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A new radioimmunoassay for the measurement of histamine in biologic fluids was evaluated. Assay selectivity and specificity were achieved by "succinyl-glycinamide derivatization" of histamine in samples to mimic the immunogen used to generate the monoclonal antibody. The assay exhibits a linear response from 0.1 to 5.0 ng/ml of histamine and the monoclonal antibody used has partial recognition of only N-methylhistamine (other than histamine). With minimal modifications, the assay can accurately measure histamine in plasma, urine, and buffer. Normal ranges for human subjects were established: plasma levels are 0.193 ± 0.08 ng/ml (n = 40) and urine levels are 20.9 ± 11.2 μg histamine/gm creatinine (n = 10). (J ALLERGY CLIN IMMUNOL 1988;82:638-46.)

Histamine is a relatively specific indicator of mast cell activation in human subjects and has been clearly implicated as a primary mediator in allergic reactions.

Many potential roles for histamine in human health and disease have been suggested, but only a few have been confirmed. Transient elevations in plasma histamine levels have been found with anaphylaxis,[1] physical urticarias after provocation,[2-4] allergy skin testing,[5] and other conditions associated with mast cell activation, whereas the diagnosis of systemic mastocytosis is suggested by persistent elevations in plasma and urine histamine levels.[10-12]

Currently, the measurement of histamine in biologic

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Rubin, D.H., Damus, K. "The Relationship Between Passive Smoking and Child Health Methodologic Criteria Applied to Prior Studies" The Yale Journal of Biology and Medicine 61:401-411, 1988.

ABSTRACT: Most studies investigating the relationship between passive smoking and child health have found a significant effect on respiratory illness and lung function. The wide range of findings is based on diverse types of studies which use multiple criteria for respiratory illness, smoke exposure, and outcome variables. The aim of this review is to examine these studies in an attempt to focus attention on methodological criteria which relate to the strength of the association and likelihood of a causal relationship between passive smoking and child health.

We examined 30 studies and judged their strength by examining (1) data collection, (2) surveillance bias, (3) definition of amount of smoking, (4) definition of illness, (5) detection bias, (6) outcome variables, and (7) control for confounding variables. Poor scores were noted in the use of "blinded" data collectors (37 percent of possible score), use of multiple specific outcome variables (51 percent), and definition of the quantity of smoking (56 percent). Good scores were noted in the detection of illnesses (98 percent), recall by study subjects of symptoms of illness (71 percent), control for confounding variables (81 percent), and definition of illnesses (86 percent). The range of scores for the studies was from 44 percent to 89 percent (of the total possible score).

While a few well-designed studies demonstrate a significant effect of passive smoking on child health, most studies had significant design problems that prevent reliance on their conclusions. Thus, many questions remain, and future studies should consider important methodological standards to determine more accurately the effect of passive smoking on child health.

The Relationship Between Passive Smoking and Child Health: Methodologic Criteria Applied to Prior Studies

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Most studies investigating the relationship between passive smoking and child health have found a significant effect on respiratory illness and lung function. The wide range of findings is based on diverse types of studies which use multiple criteria for respiratory illness, smoke exposure, and outcome variables. The aim of this review is to examine these studies in an attempt to focus attention on methodological criteria which relate to the strength of the association and likelihood of a causal relationship between passive smoking and child health.

We examined 30 studies and judged their strength by examining (1) data collection, (2) surveillance bias, (3) definition of amount of smoking, (4) definition of illness, (5) detection bias, (6) outcome variables, and (7) control for confounding variables. Poor scores were noted in the use of "blinded" data collectors (37 percent of possible score), use of multiple specific outcome variables (51 percent), and definition of the quantity of smoking (56 percent). Good scores were noted in the detection of illnesses (98 percent), recall by study subjects of symptoms of illness (71 percent), control for confounding variables (81 percent), and definition of illnesses (86 percent). The range of scores for the studies was from 44 percent to 89 percent (of the total possible score).

While a few well-designed studies demonstrate a significant effect of passive smoking on child health, most studies had significant design problems that prevent reliance on their conclusions. Thus, many questions remain, and future studies should consider important methodological standards to determine more accurately the effect of passive smoking on child health.

During the past few years, the relationship between passive smoking and child health has received substantial attention in the medical literature. Most of the evidence suggests that there is a significant causal relationship between passive smoke exposure (defined as the exposure when children are in close proximity to the smoke from burning cigarettes, pipes, or cigars, or to exhaled smoke produced by smokers) and child ill-health [1-30]. A recent Surgeon General's report highlighted the risk of exposure to the non-smoking public by those who continue to smoke [31]. While most studies have found at least some relationship between passive smoke and child health, others have found little or no effect [32-33].

Even though this topic has been the focus of many studies, it is not clear when passive exposure to smoke begins to affect child health nor the extent of the dose-effect relationship. This information is important both for (1) public policy, which could be directed against the exposure of children to smoke; and (2) research policy, which could be directed toward the newer issues in this field such as the effect of prenatal exposure to passive smoke on fetal development.

Exposure to passive smoke has been associated with reduced birthweight [34,35]

and child height [10,12]. increased incidence of childhood asthma [9,14,36], bronchiolitis [7], persistent wheezing [1], childhood cough [8,17,20,24], tracheitis and bronchitis [6], and respiratory illness in the first [18], second [22], and middle childhood years [16]. Passively inhaled smoke has also been shown to be associated with a reduction in pulmonary function in children [3,5,11].

Prospective, case-control, and cross-sectional study designs have been used to investigate the effect of passive smoking on child health. In the prospective study design, children are followed over time and examined at specific predetermined intervals; pulmonary function testing is often performed during these interval examinations and used as an outcome variable in these studies. In the case-control study design, smoke exposure is compared between those children who have or have not had a specific illness, such as bronchiolitis. In the cross-sectional study design, the strength of association between past smoke exposure and a specific outcome (i.e., cough or pulmonary function testing) at a specific time is tested.

Within any selected design, studies have demonstrated substantial differences with respect to the following: (1) the definition and quantification of smoking of all household members; (2) the accuracy of recording the amount of smoke to which a child is exposed, including in-home and outside-the-home exposure; (3) the definitions of symptoms and diagnostic criteria for respiratory illness; and (4) the measurements used to assess the effect and quantity of exposure to passive smoking. In addition, issues such as the need for "blinding" of research personnel during data collection and the frequent examination of study subjects have been addressed by only a few studies [7,21,24]. These methodologic shortcomings make it difficult to compare results of prior studies and to delineate the effect of passive smoking on child health.

Many of the problems are obvious even without critical review. Some investigators recorded smoking history by determining the number of cigarettes smoked per day by the mother and/or father (current and/or prior consumption), while others simply classified household smoking patterns as either the presence or the absence of smoking by both parents [3,26]. In other studies, researchers assigned the number of cigarettes smoked per day to a distinct category, such as 1-10, 11-20, or >20 cigarettes per day [6], or 1-14, 15-24, or >25 cigarettes per day [17].

Multiple or intermittent sources of passive smoke exposure have not been explored in prior studies. A child might spend four hours a day with a parent or other caretaker who smokes only when not in the child's presence. Would this amount of smoke exposure be the same as that experienced when the parent smokes four hours per day in the child's presence? The other case involves the parent who smokes outside the home. He or she would be categorized as a "smoker," but the child's smoke exposure would not be equivalent to that of the first case, nor to that of a child who is exposed continually to smoke by a "home smoker."

Quantitative examination of cotinine (a breakdown product of nicotine metabolism) in the urine, saliva, or blood, as a validation of exposure, has not been included in any of these studies. This chemical assessment of smoke exposure has been shown to be a reliable measure of passive smoke exposure in children [37-41].

Outcome variables have included one or more of the following: (1) symptoms and/or diagnoses of lower or upper respiratory tract illnesses (e.g., cough, bronchitis, tracheitis, bronchiolitis, pneumonia); (2) pulmonary function testing, primarily of older children; (3) height; (4) amount of functional disability; or (5) hospitalization or emergency room visits.

Definitions of respiratory illness have included self-report of symptoms of illness, review of medical records from physician's offices and/or hospital out- and inpatient sources, and categorical responses to lists of symptoms of illness. In the few studies with multiple sources of information, there have been no procedures to handle data that might differ according to the source of information (e.g., self-report, hospital records) [18,22]. Only one large prospective study contacted families at frequent intervals so that symptoms, home management, and physician contact could be accurately recorded [13].

To date, there have been no standardized methods developed to test the association between passive smoking and child health. The aim of this review is to examine specific methodologic criteria in studies investigating the relationship between passive smoking and child health. This examination may help to explain some of the variation found in these studies and provide a reference for some of the issues to be considered in future studies.

METHODS

All articles describing research which focused on the relationship between passive smoking and child health, published in the English language since 1970, were requested through the MEDLINE information service.

Articles were reviewed by the two authors independently to determine (1) the type of study, (2) the sample size, (3) the age of the study group, and (4) the outcome variables used to assess the effect of exposure to passive smoke on child health.

In addition, methodological criteria were adapted from Horwitz and Feinstein [43]. These criteria were chosen because they were important issues which may significantly affect the outcome of a study. Some of these criteria were used in a recent review of the association between breast-feeding and infection by Bauchner et al. [44].

The methodological criteria used in our review are listed below.

1. Data Collection: The Use of "Blinded" Data Collectors: It is important that research personnel know as little as possible about the details of the hypotheses being tested, and not know the smoking status of study participants during (1) pulmonary function testing and (2) the questioning of study subjects regarding symptoms of illness. This lack of information is to ensure that interviewer technique is unbiased and standardized. If the examiner knows that the subject is a heavy smoker, he or she may expect a great number of symptoms related to respiratory illness in the subjects' children compared to those of subjects who are not smokers. The result could be a falsely elevated number of symptoms detected in smokers' families, compared to non-smoking families.

2. Surveillance Bias: In many prospective studies, recall of children's symptoms of illness by parents is often used as an important outcome variable. Ideally, the period of time used for recall should be minimal. We arbitrarily defined a reasonable period of recall as at least twice in a twelve-month period.

3. Definition of Smoking Exposure: Smoke exposure can occur at (1) home, (2) day care, (3) school, or (4) wherever a child spends most of his or her time. The evaluation of this variable should also include an assessment of current and prior smoking exposure by parents, household members, and child care providers. This information is particularly important in view of the large number of children attending day care [46]. Chemical analysis of the breakdown products of nicotine metabolism is also an important element of verification of the amount of smoke exposure.

4. *Definition of Illnesses:* This category is important for generalizability of findings. Whether using reported symptoms of respiratory illness or diagnostic definitions related to upper or lower respiratory tract disease, criteria for illness should be established prior to the start of the study. This information may be obtained from self-reported results, direct interview with a subject, or abstraction of information from medical records. The methods and questions used to obtain this information should be described by study investigators.

5. *Detection Bias:* All study participants should have an equal chance for detection of the target symptom or disease by the study group interviewer or medical record abstractor. Adherence to this criterion may help to eliminate bias if children living in families where there are a lot of smokers are seen more frequently in health care facilities than children from families where there are no smokers. Children from smokers' families would show a higher number of symptoms and therefore be assumed to have a higher amount of morbidity related to the quantity of smoke exposure in the household. All children should be seen an equal number of times by members of the study team assigned to assess respiratory symptoms, measure pulmonary function, or test the chemical by-products of nicotine metabolism.

6. *The Use of Multiple Outcome Variables:* The results of multiple outcome variables will enable the investigator to compare data from multiple sources; that is, those obtained through chemical analysis or by questionnaires. This information can either strengthen the results of the study (all of the data suggests a single result) or weaken the results (conflicting results according to the source). Outcome variables in these studies include: (1) the verbal report by one or both parents of all symptoms of respiratory and other illnesses, (2) pulmonary function testing, (3) hospitalization rates, (4) disability or activity restriction, and (5) emergency room visit.

7. *Control for Confounding Variables:* The causal relationship between passive smoking and child health should be adjusted for potential confounding variables. For example, when examining the relationship between passive smoking and a symptom such as cough, it is important to recognize different potential reasons (other than exposure to cigarette smoke) for increased coughing among children in a family. Increased cough could be due to exposure to common respiratory viruses in other family members and have no relationship to passive smoke exposure. If there is a significant relationship between cough and these variables during preliminary bi-variate analysis, they should be included in appropriate multivariate analyses to determine what effect they have on the relationship between passive smoke exposure and cough.

As shown in Table 1, each study was examined for adherence to the principles of each of the seven criteria. A four-point scale was used for each criterion. A "0" score meant that the criterion was not applicable to the study. A "1" score meant there was poor adherence to the criterion. A "2" score meant there was moderate adherence to the criterion. A "3" score meant there was complete adherence to the criterion. Any disagreement between authors was resolved by consensus opinion. A "good" score was defined a priori as ≥75 percent.

RESULTS

Thirty research articles focusing on the relationship between passive smoking and child health were reviewed [1,3,5–30,32,33]. Table 2 shows the type of study, sample

TABLE 1
Scoring Guidelines for Methodological Criteria

Criteria*	Score			
	0	1	2	3
Data collection	NA	No "blinding"	Some "blinding" documented	"Blinding" documented
Surveillance bias	NA	Subjects seen less than yearly	Subjects seen yearly	Subjects seen more than once per year
Smoking	NA	Current smoking by parents	Current and prior smoking by parents	Considered child care and home exposure since conception of child
Illness	NA	No clearly defined illness categories	Minimal definitions of illness	Clearly defined illness categories with criteria
Detection bias	NA	No attempt to see all subjects	Some attempt to see all subjects	All subjects seen an equal number of times
Outcome	NA	Examined only one variable	Examined two variables	Examined PFT, symptoms, cotinine (≥ 3)
Confounding	NA	None	Control for <3 variables	Control ≥ 3 variables

*Consult text for complete definitions of criteria.
NA: not applicable
PFT: pulmonary function test

size, age of subjects, and outcome variables. Fourteen of 30 (47 percent) of the studies were prospective, and 15 of 30 (50 percent) studies were cross-sectional. One study was a case-control study. Sample sizes ranged from 276–15,000 subjects. The ages of study subjects ranged from birth to 19 years. Fourteen studies (47 percent) used pulmonary function testing, and 24 (80 percent) studies used symptoms of respiratory illness as outcome variables. Only 10 of 30 (33 percent) studies used both pulmonary function testing and reports of symptoms of respiratory illness. No studies used quantitative assessment of nicotine metabolism to validate the verbal report of smoking history by study subjects. Table 3 shows the results of the methodological criteria evaluation. Two scores were used in the evaluation of the criteria. The first was the score (0–3) for each criterion added across all studies ($n = 30$). The maximum score for any one of the seven criteria was 90. The second score was based on the performance of the individual study in each of the seven methodological criteria (total of all criteria scores/total score possible).

1. *Data Collection: The Use of "Blinded" Data Collectors:* Only two of 30 (6.7 percent) studies recognized the potential impact of biased data collection on study results. In one study "the reading aloud of all study questions without any subjectivity by the research assistant" was performed [24]. In the second study, "interviewers were not aware of study hypothesis or the case/control status of subjects" [7]. Undoubtedly other studies included this concern in data management but failed to note this fact in their publications. This criterion had the lowest score of any of the seven methodological criteria (33 of 90, or 37 percent).

2. *Surveillance Bias:* In 16 studies, subjects were evaluated once due to the use of a case-control or cross-sectional study design. Four studies (4 of 14 = 29 percent) adhered to this criterion by contacting study subjects more than once a year. Pedreira

TABLE 2
Basic Methodologic Structure of Passive Smoking Child Health Studies

Study [Reference]	Type of Study[a]	Sample Size	Age of Subjects (years)	Outcome Variables[b] PFT	Symptoms	Other
Berkey [10]	P	9,273	6-11	-	-	+
Berkey [11]	P	7,834	6-10	-	-	-
Bland [20]	CS	5,835	Secondary school	-	+	-
Bonham [19]	CS	37,000 households	0-16	-	±	+
Burchfield [14]	CS	3,482	0-19	+	+	-
Cameron [27]	CS	695	0-16	-	+	-
Charlton [8]	CS	15,000	8-19	-	+	-
Chen [29]	CS	571	8-16	-	-	-
Chen [30]	P	1,163	0-1½	-	+	-
Colley [18]	P	2,205	0-5	-	+	-
Colley [17]	CS	2,426	6-14	-	+	-
Dodge [23]	P	525	8-10	-	+	-
Ekwo [24]	CS	1,355	6-12	+	+	-
Evans [13]	CS	276	4-17	+	-	+
Fergusson [21]	P	1,180	0-1	-	+	-
Fergusson [22]	P	1,265	0-3	-	+	-
Gortmaker [9]	CS	3,072	0-17	-	+	+
Harlap [16]	P	10,672	0-1	-	+	+
Hasselblad [25]	CS	16,689	6-13	+	-	-
Lebowitz [32]	CS	1,655	0-14	-	+	-
Leeder [26]	P	2,149	0-1			
McConnochie [7]	CC	59 cases 106 controls	8.4 (mean)			
Pedreira [6]	P	1,144	0-1			
Rona [12]	P	5,903	5-11	-	-	+
Schilling [33]	CS	816	7-17	+	+	-
Tager [3]	P	444	5-9	+	+	-
Tager [5]	P	1,156	5-9	+	+	-
Tashkin [28]	CS	971	7-17	+	+	-
Ware [15]	P	10,106	6-9	+	+	-
Weiss [1]	P	650	5-9	+	+	-

[a]CC: case-control;   CS: cross-sectional;   P: prospective
[b]PFT: pulmonary function testing;   Symptoms: symptoms and/or diagnoses of respiratory illness;   Other: height, activity restriction, hospitalizations, and emergency room visits;   +: outcome variable examined;   -: outcome variable not examined

et al. were able to check all study subjects during their well-baby examinations during the first year of life [6]. Weiss et al. and Tager et al. contacted study families by telephone every two weeks for a two-year period and collected information about symptoms of respiratory disease [1,3]. Fergusson et al. contacted study subjects at four and twelve months of age [21].

3. *Amount of Smoking Exposure:* Ten studies (33 percent) examined current smoking habits of parents. Twenty studies (67 percent) examined current and prior smoking habits of parents. No study examined other potential sources of passive smoking exposure such as child care exposure. The amount of smoking was classified as either the presence or absence of smoking in each parent [23-25,27], household

TABLE 3
Results of Assessment of Passive Smoking/Child Health Studies

Study (Reference)	Methodological Criteria* and Score*							Proportional Score*	%
	1	2	3	4	5	6	7		
Berkey [10]	1	2	1	3	3	2	3	15/21	71
Berkey [11]	1	2	1	3	3	1	3	14/21	67
Bland [20]	1	0	2	3	3	1	2	12/18	67
Bonham [19]	1	0	1	3	3	1	3	12/21	57
Burchfiel [14]	1	0	2	3	3	2	3	14/18	78
Cameron [27]	1	0	1	1	3	1	1	8/18	44
Charlton [8]	1	0	2	1	3	1	3	11/18	61
Chen [29]	1	0	2	0	3	2	3	11/15	73
Chen [30]	1	1	2	2	3	2	3	14/21	67
Colley [18]	1	2	2	1	3	1	1	11/21	52
Colley [17]	1	0	2	1	3	1	1	9/21	43
Dodge [23]	1	2	1	3	3	2	1	13/21	62
Ekwo [24]	2	0	2	3	3	1	2	13/18	72
Evans [13]	1	0	1	2	3	2	3	12/18	67
Fergusson [21]	1	3	1	3	3	1	3	15/21	71
Fergusson [22]	1	2	1	3	3	1	3	14/21	67
Gortmaker [9]	1	0	1	2	3	1	3	11/18	61
Harlap [16]	1	0	2	3	3	2	1	12/18	67
Hasselblad [25]	1	0	2	3	3	2	3	14/18	78
Lebowitz [32]	1	0	2	3	3	1	1	11/18	61
Leeder [26]	1	2	2	2	3	2	2	14/21	67
McConnochie [7]	3	0	2	3	3	2	3	16/18	89
Pedreira [6]	1	3	1	3	1	1	1	11/21	52
Rona [12]	1	1	2	3	3	1	3	14/21	67
Schilling [33]	1	0	2	3	3	2	3	14/18	78
Tager [3]	1	3	2	3	3	2	3	17/21	81
Tager [5]	1	2	2	3	3	2	3	16/21	76
Tashkin [28]	1	0	2	3	3	2	3	14/18	78
Ware [15]	1	2	2	3	3	2	3	16/21	76
Weiss [1]	1	3	2	3	3	2	3	17/21	81
Proportional Score*	33/90	30/42	50/90	75/87	88/90	46/90	73/90		
%	37	71	56	86	98	51	81		

*Methodological criteria   1: Data collection;   2: Surveillance bias;   3: Smoking;   4: Illness;   5: Detection bias;   6: Outcome;   7: Confounding

*Score   0: not applicable;   1: poor adherence to criteria;   2: moderate adherence to criteria;   3: adhered to criteria

*Proportional Score = $\dfrac{\text{Total of all category scores}}{\text{Total score possible}}$

smoking pattern which included past and present smoking habits [3,15], and the total number of cigarettes smoked per day by each parent [11]. Perhaps the most extensive classification of smoke exposure was by Burchfiel et al. [14]; five measures of passive smoking were used in that study. The five were: current and past smoking habits of both parents (each parent rated either never, current, or all others), number of parental smokers during the child's lifetime (0, 1, or 2), number of current household smokers (0, 1, 2, 3, or more), and duration of parental smoking [14]. Chen and Wan Xian used the total amount of cigarette exposure (from birth) during a child's life (e.g., ten

cigarettes per day for ten years equals a total of 3,650 cigarettes/year x 10 years = 36,500 cigarettes) [29-30]. No study validated the reports of parental smoking with an analysis of the metabolites of nicotine metabolism.

4. *Definition of Illness:* Most studies defined specific criteria for respiratory illness using either symptoms of respiratory disease [17,26] or specific diagnostic categories [6,16]. Several studies used the Epidemiology Standardization Project Questionnaire [47] to record symptoms of illness [5,7,15,24,25,28,32]. Fergusson created his own a priori definitions of respiratory illness based on a diary of symptoms kept by study participants during their children's first three years of life [22].

5. *Detection Bias:* In most studies (29 of 30) (97 percent), all subjects were examined the same number of times. Only one study examined subjects an unequal number of times. In that study, illnesses which were managed at home were not surveyed [6], which could have reduced the incidence of respiratory illness detected in either the smoking or non-smoking family group. This criterion had the highest total score of any of the seven criteria (88 of 90, or 98 percent).

6. *Use of Multiple Outcome Variables:* There were a variety of outcome variables examined in studies. These included one or more of the following: pulmonary function testing, symptoms of a respiratory illness, height, activity restriction, hospitalizations, and emergency room visits. Fourteen studies (47 percent) examined one outcome variable. Sixteen studies (53 percent) included two outcome variables.

7. *Control for Confounding Variables:* Twenty-three of 30 (76.7 percent) of the studies included some adjustment of results for potential confounding variables. The variables which were considered included gestational age, maternal age, race, education, number of children in the family, family living standards, duration of breast-feeding [21], parental smoking habits, gender of child, illness in other children [26], and type of cooking gas [24]. Most of the studies that included confounding variables considered at least four different variables in their statistical analyses (equal to a score of "3" on the methodological criteria assessment).

DISCUSSION

Several recent reviews have documented the effects of passive smoking on pulmonary function and on the incidence of respiratory disease [2,45]. This study focused on the specific methods of data collection and definitions of smoke exposure, illness criteria, and outcome variables in order to determine the reason for the range of findings noted in these reviews. These methodologic differences can have significant effects on outcome and produce bias in study results.

This review demonstrates the lack of uniformity in basic issues of methodological approach to this research question. Of particular note are the poor scores of those criteria focusing on *(1)* data collection, *(2)* the number and type of outcome variables examined, and *(3)* the evaluation of all potential sources of smoke exposure in study subjects. Studies using personal interviews to evaluate symptoms of respiratory disease are highly dependent on the training of the research team. Part of this training includes methods of unbiased objective evaluation of subject responses. Furthermore, the failure to "blind" research personnel to the smoking habits of study subjects can adversely affect their responses and therefore bias results. If the examiner knows the subject is a heavy smoker, his or her questioning and evaluation of responses could be biased. In such a case, research personnel may expect more symptoms from the heavily

smoking group and may prompt those subjects more, as compared to those subjects who are not heavy smokers.

Most studies examined only one or two outcome variables, including pulmonary function testing and symptoms of respiratory illness. No study considered either infectious or non-infectious illnesses other than respiratory illnesses which may have been affected by passive smoke exposure.

Most studies examined the quantity of passive smoke exposure as the result of current and/or prior smoking habits by parents. No study addressed the issue of other sources of smoke exposure. Children can be exposed to significant amounts of passive smoke exposure outside the home. This fact is important in view of the recent increase in child care alternatives used by parents [46]. No study validated verbal reports of smoking by using a quantitative analysis of a metabolite of nicotine metabolism. In view of the reasonably good correlation between cotinine levels and reported passive smoke exposure, this relatively inexpensive assay would be of substantial value in future studies [38–41].

The reason for the wide range of effects of passive smoke exposure on child health is still unclear. Nine out of the 30 (30 percent) studies scored ≥75 percent. Those studies which had the highest score on methodological criteria generally support the hypothesis that passive smoke affects child health. McConnochie and Roghmann found passive smoking directly related to the risk of developing bronchiolitis (odds ratio = 3.21, $p = .004$) [7]. Tager et al. found a direct measurable effect of passive smoking on pulmonary function, although no relationship was found between parental smoking and respiratory illness [5]. Weiss et al. found a significant relationship between parental smoking and persistent wheeze ($p = 0.012$) and pulmonary function [2].

Therefore, even though a large number of studies have been completed on this subject, further work remains to delineate the precise "dose-effect" relationship of this toxin. Both public and research policy would benefit from a more standardized approach to research in this field. Public policy might benefit by defining the benefits reasonably to be expected from intervening at specific times to prevent ongoing exposure to passive smoke. Research policy might benefit by developing a clearer approach toward the experience of studying this toxin and applying this knowledge to other new areas in the smoking arena, such as in studies of the effects of smokeless tobacco.

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B

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PARENTAL SMOKING AND CHILDRENS' LUNG FUNCTION

LUNG FUNCTION IN CHILDREN

The studies that have investigated lung function in children and its possible relationship to environmental tobacco smoke exposure are presented in this section. To aid in the interpretation of this literature, definitions of the major lung function parameters are provided below.

Df: One of the most widely used measures of pulmonary function in adults and children is forced vital capacity and is represented in the literature as FVC. This term refers to the maximum volume of gas that a person can expire as forcefully and rapidly as possible from their lungs immediately following a maximal inspiration of air.   When a person's ability to expire air forcefully and rapidly from their lungs (FVC) is compromised, this can possibly be an indication of chronic obstructive lung disease. Decreased FVC is common in restrictive diseases such as pulmonary fibrosis and in obstructive diseases such as emphysema and asthma.

Df: A second important measure of pulmonary function is the forced expiratory volume in one second, which is abbreviated as FEV1 in the literature. The FEV1 measure is simply the amount of air that is expired in the first second of the FVC maneuver. As with FVC, this parameter is useful in the assessment of airway obstruction. The two parameters, FVC and FEV1, are often used in a ratio to determine the percentage of a person's FVC that is expired in the first second of the maneuver. A FEV1/FVC ratio lower than 65% to 70% is characteristic of obstructive lung disease. On the other hand, subjects with restrictive lung disease will often show a normal or exaggerated FEV1/FVC value.

Df: Forced expiratory flow, known as FEF25%-75%, is the average rate of flow of air during the middle half of an FEV maneuver. The FEF25%-75% is indicative of the status of the medium and small sized airways. Decreased values of FEF25%-75% are common in the early stages of obstructive lung disease. Low values of FEF25%-75% in combination with normal values of FVC and FEV1 are often indicative of early small airways abnormality. Reduced FEF25%-75% are sometimes seen in cases of severe restrictive disease as well.

All of these measures share a common problem: accurate assessment requires the full cooperation and maximal effort of the subjects under investigation. Accurate measures are sometimes

therefore difficult to obtain, especially when the subjects are young children who do not fully comprehend the requirements being made of them in the pulmonary function tests. The studies are not consistent in the lung function parameters they measure, and there is also a lack of consistency among the results of the same function tests across studies. Following is a presentation of the major studies that have examined these lung function parameters in children. The investigators who have found associations between impaired lung function and ETS exposure are often uncertain of the clinical meanings of the small decreases observed in their studies. Therefore, it is not suprising that no definitive conclusions have been reached regarding ETS exposure and its possible association with lung function in children.

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RESULTS OF SELECTED STUDIES: CHILDHOOD LUNG FUNCTION

STUDY	EFFECT ON FEV1, FEV.75	EFFECT ON FEF25-75%
Tager 1976	decrease	not reported
Tager 1979	none	decrease
Weiss 1980	none	decrease
Tager 1983	decrease 7%	none
O'Connor 1987	decrease 5-7%	decrease 14-15%
Ware 1984	decrease .6-.9%	not reported
Berkey 1986	decrease .85%	not reported
Hasselblad 1981	decrease .5-2%	not reported
Tashkin 1984	none	decrease 2.5%
Ekwo 1983	none	none
Vedal 1984	none	decrease 4%
Spinaci 1985	decrease	none
Chen 1986	decrease 3%	decrease 6%
Burchfiel 1986	decrease 4-5%	not reported
Yarnell 1979	decrease 3%	decrease 12%
Teculesco 1986	decrease 5%	not reported
Tsimoyianis 1987	not done	decrease
Lebowitz 1987	none	not done
Leeder 1976	not done	not done
Schilling 1977	none	not reported
Speizer 1980	none	not reported
Dodge 1982	none	not reported
Lebowitz 1984	none	not reported
Lebowitz 1984	not done	not done

Adapted from Witorsch 1989

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ABSTRACT. The clinical condition and lung function of 14-year-old
schoolchildren from three different districts of Budapest were
recorded monthly between November 1972 and May 1973. R_{aw} and SG_{aw}
values and lung volumes were measured and air pollution was recorded
simultaneously. The latter differed significantly in the three
districts. Although there were significant differences between
the monthly lung function values and monthly air pollution, there
was no evidence of any connection between the function values and
environmental factors.

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Relationship between Lung Function Values and Air Pollution Data, in Budapest Schoolchildren *

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Abstract. The clinical condition and lung function of 14-year-old schoolchildren from three different districts of Budapest were recorded monthly between November 1972 and May 1973. R_{aw} and SG_{aw} values and lung volumes were measured and air pollution was recorded simultaneously. The latter differed significantly in the three districts. Although there were significant differences between the monthly lung function values and monthly air pollution, there was no evidence of any connection between the function values and environmental factors.

Key words: Schoolchildren — Environmental Factors — Lung Function Values.

The correlation between air pollution and respiratory diseases has become a very topical subject for study ever since the "smog catastrophe" in London in 1952 [29]. Many results have demonstrated a close correlation between air pollution and meteorological factors on the one hand, and respiratory complaints [8, 17, 20, 24, 36, 40, 43], respiratory morbidity [1, 3, 4, 9, 13, 16, 17, 20, 32, 41], mortality [3, 9, 20, 29] and respiratory function values [6, 15, 16, 17, 20, 28, 37, 38, 39, 43, 44] on the other particularly in young children, school-children, the elderly and in patients with chronic respiratory diseases [1, 3, 9, 13, 37, 40, 43, 44]. The causal role of smoking, social factors, the "urban factor" and respiratory infections in adolescence have also been emphasized in respect of the development of chronic bronchial diseases [5, 8, 10, 14, 22, 24, 35]. On the other hand, other authors have failed to demonstrate any such relationship with respiratory complaints [11, 15, 26] or respiratory function [2, 18, 23, 30, 33, 34].

In order to establish the short-term and long-term effects of air pollution and meteorological factors on the respiratory system, between November 1972 and May 1973 we carried out serial tests on 14-year-old schoolchildren in Budapest.

Material and Method

Three classes were selected from different parts of the city. The first school was in the centre of the city where air pollution and population density are at their greatest; the second was on the edge of an industrial area in the middle of a new housing estate, and the third school was in a non-industrialized suburb where the population density was fairly low (Fig. 1).
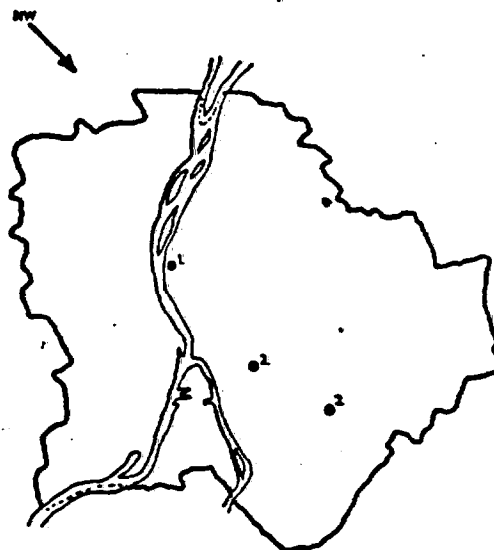
Fig. 1. The locality of the measuring stations and the schools. The population density in each district. Density of population: 1. = 23938, 2. = 8611, 3. = 2301; ● = air sampling station

The three classes (VIIIth class of the primary school) contained 86 children. These children were examined once a month from November to May, seven times in all. The Hungarian educational system is to send the children of each district to specific primary schools, and so the children are representative of the population of that district. Air pollution in the vicinity of the schools was monitored throughout the period of the investigation.

Before the examinations, we prepared a questionnaire for each child in which we recorded previous diseases, school absences for respiratory ailments, details of home conditions and the parents' smoking habits and, possibly, those of the children. Each month the children were examined clinically and their lung function was tested.

For analysing lung function we used a volume-constant body plethysmograph (Bodytest, Jaeger Co., Würzburg). Intrathoracic gas volume (ITGV) and total airway resistance (R_{aw}) were determined by the plethysmography principle, and vital capacity (VC) from the integrated pneumotachygram. Total lung capacity (TC), residual volume (RV, RV·100/TC) and specific conductance values ($SG_{aw} = R_{aw}^{-1} \cdot ITGV^{-1}$) were calculated from the above parameters. Each month we also recorded the respiratory ailments, any respiratory disease and absences from school.

We measured the monthly mean readings for SO_2, NO_2 and Cl_2 concentration and the amount of dustfall, and the daily readings for SO_2, NO_2 and Cl_2 concentrations, and simultaneously recorded the meteorological parameters, outside temperature, humidity and barometric pressure. Monthly means for SO_2, NO_2 and Cl_2 concentration were calculated from samples exposed for 20 minutes. Samples were collected eight to ten times a month at the same time at all measuring stations (between 11.0 a.m. and 2.0 p.m.). We used the pararosaniline method to determine the SO_2 concentration. NO_2 concentrations were measured by the sulphanilic acid-alpha-naphthylamine method and Cl_2 concentrations by the Na-arsenite-silver nitrate method. The concentrations are stated in mg/m^3. We measured dustfall continuously, and stated the dust levels in $g/m^2/month$.

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The results were analysed statistically by variance analysis, variance analysis for two-way classification and by random block analysis.

Results

The expected correlation between the monthly means for SO_2 concentration and the seasonal or heating periods was in fact demonstrated. SO_2 concentrations varied in the districts studied, the highest levels being found in the middle of the city around the first school (mean monthly value being 0,91 mg/m³ in December) and the lowest levels in the suburb, around the third school (Fig. 2). There were no seasonal or local differences between NO_x and Cl_2 concentrations. The maximum mean monthly NO_x concentration was 0,19 mg/m³ and the Cl_2 concentration 0,36 mg/m³. There were very large fluctuations in the levels of dustfall in the vicinity of the first and second schools (maximum 37 and 38 g/m²/month, respectively). The fluctuations were not seasonal. There were fairly small fluctuations and low absolute readings in the vicinity of the third school, the maximum being 6 g/m²/month. Temperature and humidity showed the usual seasonal variations with a minimum temperature and maximum humidity in January (−0,7° C, 86%) and with the reverse maximum and minimum levels in May (+17,1° C, 55%).

Table 1 shows the children classified according to school and sex, with the corresponding Broca Index values. There was no significant difference between the Broca Index values for schoolchildren from the different schools (Table 1).

There was no significant difference between the ITGV, R_{aw} and SG_{aw} values for boys and girls. On average, vital capacity was about 400 ml higher in the boys than in girls in all classes. The mean R_{aw} values were higher than those reported in the literature for healthy adults [31].

We did not find any significant difference between the mean R_{aw} values in the three classes. These means were calculated from seven measurements. The results of
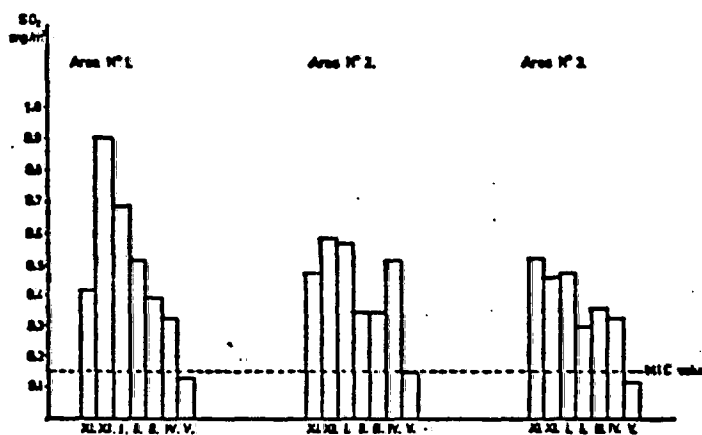

Fig. 2. The monthly means for SO_2 concentration (mg/m³) from November 1972 to May 1973 in the three measuring stations

Table 1. The number of children in each class. Broca Index

	GIRLS	BOYS	TOTAL	BROCA INDEX
SCHOOL N° 1	18	12	30	80
SCHOOL N° 2	13	15	28	82
SCHOOL N° 3	15	13	28	80

Table 2. The monthly means for total airway resistance (R_{aw}) in the three classes fro. November 1972 to May 1973. Statistical results. p values at the end of the lines show th results of variance analysis. p value below the mean annual values shows the level c significance between the three means

	NOV	DEC	JAN	FEBR	MARCH	APR	MAY	Mean annual values	p %
School N° 1	2.487	2.728	2.558	2.471	2.428	2.777	2.250	2.570	< 5
School N° 2	2.531	2.255	2.718	3.177	2.849	2.664	2.824	2.738	< 5
School N° 3	2.319	2.351	2.706	2.804	2.925	2.183	2.308	2.614	< 5
N° 1 - N° 2	p < 5	p < 5	p > 5	p < 5	p < 5	p > 5	p < 5		
N° 1 - N° 3	p < 5	p > 5	p > 5	p > 5	p < 5	p > 5	p > 5	p > 5	
N° 2 - N° 3	p > 5	p > 5	p > 5	p > 5	p > 5	p > 5	p < 5		

Table 3. Means for vital capacity (VC), residual volume (RV), total capacity (TC) and intrathoracic gas volume (ITGV) for each of the classes with monthly minima and maxima Statistical results

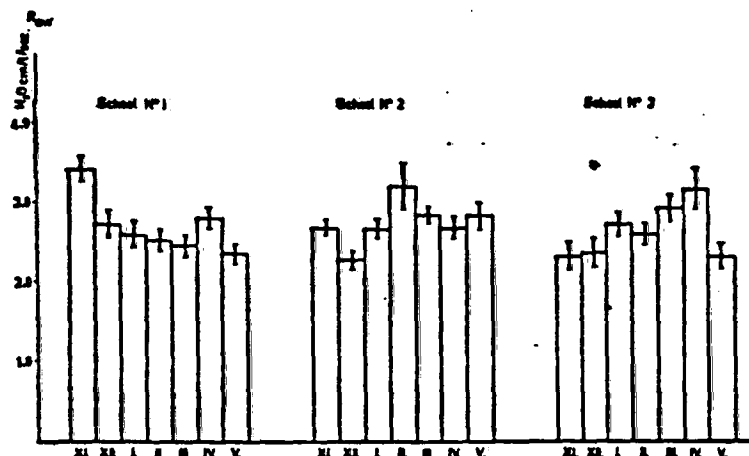|	SCHOOL N° 1	p%	SCHOOL N° 2	p%	SCHOOL N° 3	p%
VITAL CAPACITY (ml)	3386 (3268Nov) - 3678(Dec)	< 5	3280 (3142(Jan) - 3488(Dec)	> 5	3568 (3336(Jan) - 3864(Dec)	< 5
RESIDUAL VOLUME (ml)	1405 (1068(Dec) - 1823(May)	< 5	1276 (884(Dec) - 1688(Jan)	< 5	1361 (872(Dec) - 1988May)	< 5
TOTAL CAPACITY (ml)	4796 (4258 Nov) - 5828March)	< 5	4541 (3983Dec) - 5798May)	> 5	4924 (4363(Apr) - 5862May)	> 5
INTRATHORACIC GAS VOLUME (ml)	2588 (2062Dec) - 2773March)	< 5	2366 (2220Dec) - 2548March)	> 5	2635 (2483Nov) - 2853May)	> 5

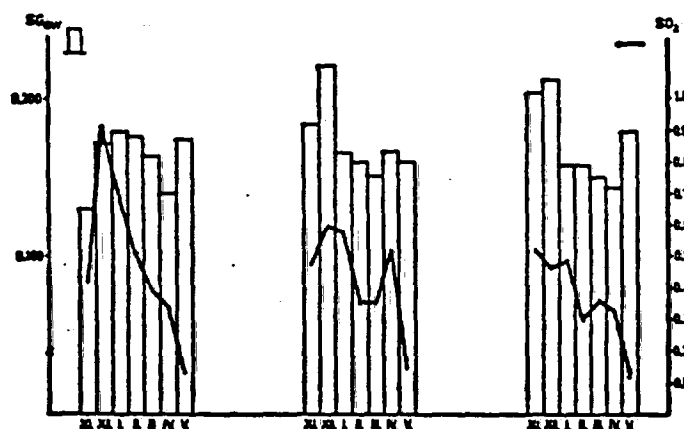Fig. 3. The means for resistance to flow (R_{aw}) in the three classes from November 1972 to May 1973

Fig. 4. The monthly means for SO_2 concentration in the three measuring stations and specific conductance (SG_{aw}) in the three classes from November 1972 to May 1973

variance analysis indicate that the mean R_{aw} readings for individual classes were statistically heterogeneous during the investigation. There were significant differences between the monthly means in all classes. These differences also appeared in individual months between the three classes (Table 2). However, although in two classes the R_{aw} values were actually lowest in May, there were no definite connections between season or locality and the SO_2 concentrations—air temperature and humidity values (Fig. 3). There were similar fluctuations of the SG_{aw} values (Fig. 4).

Table 4. Statistical results of variance analysis for two-way classification of respira function parameters

		F	p%
VC	SCHOOL	12.52	< 5
	MONTH	6.95	< 5
ITGV	SCHOOL	15.48	< 5
	MONTH	4.77	< 5
TC	SCHOOL	11.65	< 5
	MONTH	3.57	< 5
RV	SCHOOL	3.71	< 5
	MONTH	14.70	< 5
R_{aw}	SCHOOL	0.78	> 5
	MONTH	2.36	> 5
SG_{aw}	SCHOOL	1.62	> 5
	MONTH	4.96	< 5

Table 5. Results of random block analysis of respiratory function parameters

		SCHOOL N° 1 n=17		SCHOOL N° 2 n=13		SCHOOL N° 3 n=21	
		F	p%	F	p%	F	p%
VC	children	32.35	< 5	64.23	< 5	72.40	< 5
	month	45.54	< 5	12.41	< 5	22.67	< 5
ITGV	children	11.38	< 5	24.20	< 5	28.01	< 5
	month	4.86	< 5	4.23	< 5	6.12	< 5
TC	children	15.95	< 5	28.81	< 5	38.78	< 5
	month	9.23	< 5	4.53	< 5	1.50	> 5
RV	children	3.64	< 5	6.18	< 5	5.89	< 5
	month	4.58	< 5	6.42	< 5	10.30	< 5
R_{aw}	children	6.79	< 5	3.22	< 5	8.17	< 5
	month	5.77	< 5	2.60	< 5	4.30	< 5
SG_{aw}	children	4.62	< 5	3.33	< 5	8.95	< 5
	month	3.40	< 5	4.60	< 5	5.24	< 5

There were significant differences between the monthly ITGV and spirometric means, but there was no evidence of a connection with environmental factors (Table 3).

There was no connection between the daily readings for environmental factors and lung function parameters. By performing variance analysis for two-way classification on the whole of the material, we demonstrated that the fluctuations in respiratory function values are affected more by seasonal factors than by locality factors. The two factors mentioned above do not have a significant effect on the scatter of R_{aw} values; the scatter of SG_{aw} values depends solely on time factors. These results demonstrate that the latter parameters of respiratory function are more stable (Table 4).

The results from the children who took part in all the investigations were evaluated by random block analysis. The numbers were 17, 13, and 21 in the first, se-

cond and third class. The analysis verified that the significant differences were affected more by the variations in measurement results between individual children, than by the fluctuations in respect of time in the same children. These results also showed that R_{aw} and SG_{aw} values were the most stable (Table 5).

We did not find any connection between air pollution and respiratory complaints clinical condition and school absences caused by respiratory diseases. The latter was highest in February in all classes (coinciding with a mild influenza epidemic). Similarly, there was no connection between home conditions, smoking habits of the parents and respiratory function values.

Discussion

From the results we concluded that the respiratory function values, respiratory complaints and respiratory symptoms of healthy 14-year-old schoolchildren were neither affected permanently nor periodically by the prevailing level of air pollution. In our opinion, there is no permanent effect. This is based on the homogenity of the means for R_{aw} from the three classes. Since there is no definite correlation between air pollution levels as a function of time, and respiratory function values, we also doubt the short-term effect. It must be emphasized that the SO_2 concentration and meteorological conditions during the period of the survey did not show any extreme variations like those which occurred during the "smog catastrophe", although the SO_2 concentrations were far above normal, healthy standards. Presumably the significant fluctuations in the monthly means of some parameters were caused by other exogenous factors not studied as yet. Presumably also, the effects of environmental factors would be easier to detect in younger children or in the elderly and sick people. It is also possible that the methods we used are unsuitable for diagnosing very early changes in the peripheral airways. However, some of the more recent diagnostic techniques are still not completely satisfactory from the theoretical point of view, and we still know nothing about the importance of changes in the peripheral bronchi from the point of view of clinical prognosis [3, 5, 7, 12, 21, 25, 28, 42, 44]. We consider that, in view of the greater stability of the R_{aw} and SG_{aw} levels, these parameters should be suitable for serial studies. Thus, in our view, the effects of air pollution on the respiratory system have not been fully elucidated. The unanswered questions can only be answered by undertaking longitudinal and vertical studies on larger populations, using suitable methods.

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"Household Aggregation of Pulmonary Function and Chronic Bronchitis"
American Review of Respiratory Disease 114:   485-492, 1976.

SUMMARY: Persons from 148 randomly selected households in an urban
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significantly correlated between siblings, but less clearly so
between spouses. Correlation of 1-sec forced expiratory volume
between mother and child appeared to be confounded by maternal
smoking habits, an effect most notable between mothers and male
offspring. The 1-sec forced expiratory volume of fathers was
significantly correlated with that of their children, especially
female children, an effect that appeared to be independent of
smoking habits.

Household Aggregation of Pulmonary Function and Chronic Bronchitis[1][2]

IRA B. TAGER, BERNARD ROSNER, PETER V. TISHLER,
FRANK E. SPEIZER,[4] and EDWARD H. KASS

SUMMARY

Persons from 148 randomly selected households in an urban community were screened in their homes using a modified British Medical Research Council respiratory disease questionnaire and a portable spirometer. Analysis showed a significant tendency for chronic bronchitis to aggregate within households. Significant aggregation was observed for 1-sec forced expiratory volume, when measured as the per cent of the predicted value or as a score calculated from the data. The 1-sec forced expiratory volume was significantly correlated between siblings, but less clearly so between spouses. Correlation of 1-sec forced expiratory volume between mother and child appeared to be confounded by maternal smoking habits, an effect most notable between mothers and male offspring. The 1-sec forced expiratory volume of fathers was significantly correlated with that of their children, especially female children, an effect that appeared to be independent of smoking habits.

Introduction

The possibility that familial factors (apart from α_1-antitrypsin abnormalities) may be important in the pathogenesis of chronic bronchitis and obstructive airway disease has received relatively little attention in the otherwise extensive literature dealing with these entities. In one of the earliest modern investigations, Oswald and associates (1) noted that relatives of persons with

chronic bronchitis had a rate of bronchitis 3 times that of the relatives of persons without chronic bronchitis. Ogilvie and Newell (2) found that a family history of bronchitis was twice as common among persons with bronchitis than among persons without bronchitis. However, these investigators were unable to find any evidence for the clustering of bronchitis within given households. Studies in monozygotic twins have demonstrated a significant concordance in the occurrence of chronic cough; moreover, the correlation was clearly independent of cigarette smoking (3). Studies in Tecumseh, Mich. have shown a familial tendency for the occurrence of chronic respiratory disease, as well as significant correlation between levels of pulmonary function in parents and their children and among siblings, regardless of sex (4). Household-familial aggregation of bronchitis has also been observed by Colley (5) in a study that focused on the occurrence of bronchitis in children.

The data presented here were collected as part of a series of studies designed to describe the occurrence of chronic bronchitis and obstructive airway disease in a defined urban population and to identify host and environmental factors

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that are associated with the observed prevalence of these entities. Our data support the concept of an important household-familial aggregation of chronic bronchitis.

Materials and Methods

Selection of sample. The study sample was drawn from the population of East Boston, Mass., a geographically distinct area of Boston inhabited largely by Italian-Americans. In 1970, a 3.5 per cent cluster-sample of this population was selected based on census blocks compiled by the police. This sample was drawn as part of a Hypertension Detection and Follow-up Program sponsored by the National Heart and Lung Institute. All households on the selected blocks were canvassed by trained home visitors, and the residents of each household were enumerated for the sample. The final sample contained 1,159 persons and 486 households, of which 358 contained at least 2 members.

Screening of sample. Between January 1975 and March 1974, persons living in the selected households were visited by trained home visitors. All households were visited at least 2 subsequent times if subjects were not reached. A modified version of the standard British Medical Research Council questionnaire was administered to the appropriate household members, either directly (for subjects more than 12 years of age) or indirectly (for subjects ≤ 12 years of age) through parents. The questionnaire included the standard questions on cough, phlegm, and chest illnesses, as well as an expanded section on smoking and other respiratory illnesses. Forced vital capacity (FVC) maneuvers were performed on a portable, water-filled, 8-liter spirometer (Warren Collins, Inc., Braintree, Mass.). Each subject performed FVC maneuvers in the sitting position, without noseclip, until 5 acceptable tracings (tracings of at least 6-sec duration, and adequately performed, as determined by the home visitor) were obtained. Standing height was measured without shoes to the nearest 0.5 inch. Based on the questionnaire, persons who reported cough and phlegm for at least 3 months per year were considered to have simple chronic bronchitis.

Assessment of pulmonary function. The five FVC tracings were corrected to BTPS. The mean values of the 3 best tracings were used to derive the working FVC and the 1-sec forced expiratory volume (FEV$_1$). The FEV$_1$ per cent predicted was calculated from the nomograms of Ferris and associates (8) for subjects 25 or more years of age, and from those of Dickman and associates (7) for subjects 5 to 24 years of age. Regressions calculated from our data were not significantly different from those obtained by Ferris and associates (8) and Dickman and associates (7). Male and female subjects were divided into the age groups, 5 to 24 years, and 25 years and

older. For each age-sex group, a regression of FEV$_1$ on age and height was obtained, using only subjects without chronic bronchitis or obstructive airway disease. For each subject, a standard FEV$_1$ score was generated according to the formula,

$$\text{FEV}_1 \text{ score} = \frac{(\text{observed FEV}_1) - (\text{age-sex specific predicted FEV}_1)}{\text{standard error of estimate for age-sex specific regression}}$$

This score was found to be distributed approximately normally around a mean of zero, with unit variance.

Analysis of data. Households were included in the analysis if complete historical and functional data were available for more than 60 per cent of the household members. Households with 2 persons were included only if complete data were available for both subjects. Information concerning age, sex, and smoking habits was available from another source (Hypertension Detection and Control Contract N01-HV-12433 from the National Heart and Lung Institute) for 95 per cent of the nonparticipants in this study. These data were compared to those for subjects for whom data were available to ascertain obvious biases in the participating subject group.

To test the hypothesis of household aggregation of chronic bronchitis, a multivariate logistic model was used (8). Age, sex, and lifetime cigarette consumption were used to obtain the probability of occurrence of chronic bronchitis for each subject. Based on these probabilities, an expected number of cases was obtained for each household. The observed number of cases in a household was assumed to follow a Poisson distribution, with the parameter equal to the expected number of cases obtained from the logistic model. For each household, the percentile of this distribution corresponding to the actual number of cases observed was computed. The observed percentiles were accumulated for all households and were then grouped by decile. A chi-square goodness of fit test was then used to compare the observed number of households in the deciles with an expected uniform distribution, which would have been obtained if no household aggregation were present.

Intraclass correlation coefficients were calculated according to the method of Smith (9). This method provides a weighted estimate of the intraclass correlation and an accompanying standard deviation for the situation in which the size of the groupings is not fixed. Correlation coefficients (product-moment) (10) between parents (mother, father, and midparent, i.e., the value for mother plus value for father divided by 2), and their children were calculated assuming each parent-child pair to be independent. Standard normal deviates based on sex-specific 5-year (subjects 5 to 24 years of age) and 10-year (subjects 25 years of age and older) age groups were used in calculating the correlation coefficients for height. Regression analyses were carried out according to standard procedures (11).

each age-sex group, a regression of FEV_1 height was obtained, using only subjects ronic bronchitis or obstructive airway dis- ach subject, a standard FEV_1 score was ccording to the formula,

$$\frac{\text{(observed } FEV_1) - \text{(category-specific predicted } FEV_1)}{\text{standard error of estimate for category-specific regression}}$$

ras found to be distributed approximately ound a mean of zero, with unit variance. of data. Households were included in the complete historical and functional data ble for more than 60 per cent of the house- ers. Households with 2 persons were in- if complete data were available for both ormation concerning age, sex, and smok- ras available from another source (Hy- Detection and Control Contract N01-HV- the National Heart and Lung Institute) ent of the nonparticipants in this study. were compared to those for subjects for vere available to ascertain obvious biases pating subject group.

e hypothesis of household aggregation ronchitis, a multivariate logistic model l. Age, sex, and lifetime cigarette con- re used to obtain the probability of oc- chronic bronchitis for each subject. se probabilities, an expected number of ained for each household. The observed aces was assumed to ison distribution, with the parameter xpected number of cases obtained from model. For each household, the percen- distribution corresponding to the actual ses observed was computed. The ob- tiles were accumulated for all house- ere then grouped by deciles. A chi -re of fit test was used to compare number of households in the deciles ed uniform distribution, which would ained if no household aggregation were

rrelation coefficients were calculated the method of Smith (9). This meth- weighted estimate of the intraclass l an accompanying standard deviation e in which the size of the groupings is elation coefficients (product-moment) arents (mother, father, and midpar- due for mother plus value for father and their children were calculated parent-child pair to be independent. al deviates based on sex-specific 5- 5 to 24 years of age) and 10-year rs of age and older) age groups were using the correlation coefficients for ion analyses were carried out accord- procedures (11).

Results

The original sample was composed of 1,159 subjects in 338 households. Of this number, 13.1 per cent (152 of 1,159) had moved before the on- set of the study, and 11.6 per cent (134 of 1,159) could not be located after at least 3 visits to the household. Data were obtained for 633 of the remaining 873 subjects (72.5 per cent). One hundred forty-eight complete households were available for analysis from this group (table 1). These households represent 469 subjects, or 74 per cent of the total (469 of 633). Twenty-nine per cent (24 of 84) of households with more than 2 members did not have 100 per cent par- ticipation. In all but 2 instances, data were available for all but one member of the house- hold (table 1). In comparison with the house- holds that were not available for analysis, dif- ferences were observed in the number of mem- bers per household (mean of 3.4 in participating households versus 2.7 among nonparticipants; $X_4^2 = 16.59$; $P < 0.01$); the number of rooms per household (respective means of 5.6 and 5.1); and in age distribution (under-representation of age groups 10 to 14 years, and 45 to 54 years among participants). No significant differences were obtained for sex distribution, current ciga- rette smoking status, the duration of smoking, or the total lifetime consumption of cigarettes. The average age of the children within the households was 13.8 ± 5.6 years (range, 5 to 31 years).

Application of the logit analysis resulted in a highly significant tendency for chronic bron- chitis to cluster within households ($X_9^2 = 90.72$;

$P < 0.001$). Similar analysis was not attempted for obstructive airway disease because of the small number of cases available for analysis.

Level of pulmonary function showed a signifi- cantly greater similarity within households than among members of different households (table 2). Further analysis revealed that levels of pul- monary function for both FEV_1 per cent pre- dicted and FEV_1 score were significantly associa- ted among siblings, but not between husbands and wives (table 2). Similar associations were seen with the intraclass and product-moment correlation of coefficients (table 3). With eith- er measure of pulmonary function, there was a highly significant correlation of level of pulmo- nary function among siblings (intraclass corre- lation coefficient, $\rho = 0.26$ for FEV_1 per cent predicted; $\rho = 0.19$ for FEV_1 score). Between spouses, no such correlation could be found us- ing the product-moment correlation coefficient ($r = 0.039$ for FEV_1 per cent predicted; $r = 0.052$ for FEV_1 score); however, for 29 spouse pairs in which both members were either cur- rent smokers or had never smoked, the correla- tion coefficient for FEV_1 per cent predicted was 0.53 ($t = 1.80$; $P < 0.1$). When the children included in the analysis were randomly reas- signed to nonbiologic parents, producing a distribution of sibship sizes identical to that found in the actual sample, the intraclass corre- lation coefficient for FEV_1 per cent predicted was no longer significant ($\rho = 0.06 = 0.08$; $P = 0.45$).

For mother-child pairs, there was a significant correlation for FEV_1 per cent predicted, but

TABLE 1

DISTRIBUTION OF HOUSEHOLD SIZES FOR HOUSEHOLDS AVAILABLE FOR ANALYSIS

Household Size	Total No. In Sample	No. In Analysis	No. with 100% Participation
2	171	64	64
3	69	25	20*
4	48	26	20*
5	32	21	12†
6	12	8	6*
7	2	1	1
8	2	1	0*
10	2	2	1*
Total	338	148	(469 subjects)

*No data were available for one member of each household.
†No data were available for one member of 7 households; no data were available for 2 members of households.

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TABLE 2

RESULTS OF ANALYSIS OF VARIANCE FOR LEVEL OF
PULMONARY FUNCTION WITHIN HOUSEHOLDS

Household Members Included in Analysis	N	F Values FEV_1 % Predicted	F Values FEV_1 Score
All members, all households	413	1.31*	–
All members, households of 3 or more persons	270	1.64†	1.62†
All sibships	150	2.23†	1.63*
Husband-wife	160	1.16**	1.12**

*$P < 0.05$.
†$P < 0.01$.
**$P > 0.05$.

not for FEV_1 score (table 4). For the father-child and midparent-child pairs, correlations were significant for both measures of pulmonary function (table 4). The midparent-child correlation for FEV_1 per cent predicted showed the highest correlation ($r = 0.41$), a value similar to that found for the height correlations. In all 3 parent-child categories for FEV_1 per cent predicted, female children showed a stronger correlation with their parents than did male children. In no case was the correlation for male children significant for FEV_1 per cent predicted. Random reassignment of all children without regard to sex eliminated the significance of all of the correlation coefficients for FEV_1 per cent predicted.

A significant inverse correlation was found between the amount of lifetime cigarette consumption (expressed as $\log_{10}$ of lifetime consumption, to normalize the distribution, which was skewed toward large values) of mothers and the level of pulmonary function in their children, when analyzed without regard to sex of the child ($r = -0.50$ and $P < 0.01$ for FEV_1 per cent predicted; $r = -0.17$, $P = 0.04$ for FEV_1 score). This inverse correlation could not be explained solely by the smoking habits of the

children included in the analysis, because 26 per cent (27 of 104) of the children of mothers who were present or ex-smokers were themselves smokers, versus 17 per cent (6 of 35) of the children of mothers who had never smoked ($P = 0.24$ for the difference). In addition, regression analysis combining male and female children revealed a significant inverse association between maternal smoking habits (expressed as either lifetime amount consumed or smoking status, defined as ever or never smoked) and FEV_1 per cent predicted in their children. This inverse correlation persisted even when the smoking status of the children was accounted for in the analysis (table 5). The highest inverse correlations were found in the regressions that included data for both maternal and child smoking habits (table 5). Analysis by sex of child (table 6) revealed that the inverse correlation with maternal smoking occurred only for male children. Because of the small numbers involved, the sex-specific regression coefficients for both male and female "child's smoking history" were not significant, and they were not significantly different from each other ($P = 0.86$ for difference). Maternal FEV_1 per cent predicted was not independently associated with male or

TABLE 3

CORRELATION COEFFICIENTS FOR LEVEL OF
PULMONARY FUNCTION

Relationship	N	Correlation Coefficient*	SD	P Value
Siblings	150			
FEV_1 % predicted		0.26	0.09	0.004
FEV_1 score		0.19	0.09	0.035
Spouses	160			
FEV_1 % predicted		0.039	–	> 0.5
FEV_1 score		0.052	–	> 0.5

*Interclass correlation coefficient (ρ) for siblings; product-moment correlation coefficient for spouses.

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THIN HOUSEHOLDS

F Values FEV₁,% Predicted	F Values FEV₁ Score
1.31*	-
1.64†	1.62†
2.23†	1.63*
1.15**	1.12**

ildren included in the analysis, because 26 per
nt (27 of 104) of the children of mothers who
re present or ex-smokers were themselves
okers, versus 17 per cent (6 of 35) of the
ildren of mothers who had never smoked (P
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tween maternal smoking habits (expressed as
ther lifetime amount consumed or smoking
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th male and female "child's smoking history"
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antly different from each other (P = 0.86 for
ifference). Maternal FEV₁ per cent predicted
as not independently associated with male or

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rrelation efficient*	SD	P Value
0.26	0.09	0.004
0.19	0.09	0.035
0.039	-	> 0.5
0.052	-	> 0.5

ilings; product-moment correlation co-

female child FEV₁ per cent predicted in the
regression analysis (table 6). A similar regres-
sion analysis for fathers failed to demonstrate a
significant inverse correlation of paternal smok-
ing habits with child's FEV₁ per cent predicted.
Paternal FEV₁ per cent predicted was, however,
the most significant predictor (P < 0.05) of a
female child's FEV₁ per cent predicted, even

when the smoking habits of the fathers and their
female children were included in the analysis.
For male children, the regression coefficient for
paternal FEV₁ per cent predicted was not signi-
ficant. Children from households in which fa-
thers were interviewed were similar to those
from households in which mothers were inter-
viewed, in terms of age (13.4 ± 5.5 versus 13.6

TABLE 4

**PRODUCT-MOMENT CORRELATION COEFFICIENTS FOR LEVEL OF
PULMONARY FUNCTION BETWEEN PARENTS AND CHILDREN**

Relationship	No. of Pairs*	r, FEV₁,% Predicted	r, FEV₁ Score	r, Height
Mother-child	140	0.19†	0.11 (NS**)	0.36††
Mother-male child	77	0.09 (NS)***	-	-
Mother-female child	63	0.23 (NS)***	-	-
Father-child	119	0.25††	0.16†	0.29††
Father-male child	67	0.17 (NS)	-	-
Father-female child	52	0.34†	-	-
Midparent-child	94	0.41††	0.17†	0.39††
Midparent-male child	50	0.25 (NS)	-	-
Midparent-female child	44	0.51††	-	-

*In each household, each parent-child pair was treated as an independent pair.
†P < 0.05.
**Difference not significant.
††P < 0.01.
***P > 0.1 for male subjects; 0.1 > P > 0.05 for female subjects.

TABLE 5

**REGRESSIONS* OF CHILDREN'S 1-SEC FORCED EXPIRATORY VOLUME (FEV₁), EXPRESSED AS
PER CENT PREDICTED, ON MEASURES OF MATERNAL AND
CHILD CIGARETTE-SMOKING HABITS
(BASED ON 140 MOTHER-CHILD PAIRS)**

Maternal Lifetime Consumption†	Maternal Smoking History**	Maternal FEV₁,% Predicted	Maternal Smoking History**	Constant	Standard Error of Estimate	Coefficient of Determi- nation	F Value for Regression
-1.90***	-	-	-7.28†††	111.58	14.45	0.14	10.48†††
-	-9.91***	-	-6.11***	111.38	14.64	0.12	8.97†††
-	-	0.12††	-7.44***	92.93	14.92	0.08	5.61***
-	-8.42***	0.10††	-	98.75	14.87	0.08	8.13***
-1.84***	-	0.09††	-	100.90	14.72	0.10	7.59†††
-	-	0.15***	-	88.29	15.26	0.03	4.70***

*Each row of the table represents a separate regression. For each, the child's FEV₁ per cent predicted is the
dependent variable, and the variables listed under "Regression Coefficients" are the independent variables.
†Raw data were log₁₀ transformed.
**Never or ever smoked.
††P > 0.05.
***P < 0.05.
†††P < 0.01.

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TABLE 6

SEX-SPECIFIC STEPWISE REGRESSIONS OF CHILDREN'S 1-SEC FORCED
EXPIRATORY VOLUME (FEV$_1$), EXPRESSED AS PER CENT PREDICTED,
ON MEASURES OF MATERNAL AND CHILD CIGARETTE-SMOKING HABITS

	Maternal Lifetime Consumption	Maternal Smoking History	Maternal FEV$_1$ % Predicted	Child Smoking History	Constant	Standard Error of Estimate	Coefficient of Determination	F Value for Regression
Male-child (77 pairs)	−4.79*	15.60†	−0.01†	−5.10†	107.77	11.75	0.22	4.97**
Female-child (83 pairs)	−0.166†	−††	0.13†	−6.14†	102.40	16.47	0.11	2.47†

*P < 0.05.
†P > 0.05.
**P < 0.01.
††Contribution to regression so low that variable was automatically excluded in the stepwise regression.

± 5.6), proportion of male children (0.56 versus 0.55), and proportion of children who had ever smoked cigarettes (0.24 versus 0.26).

Discussion

The present data have been collected as part of an urban population-based study of chronic bronchitis and obstructive airway disease. The families included in the analysis were, on the average, larger and showed some differences in age distribution from those not included. They were, however, identical with regard to smoking habits. The biases introduced by differing household size and age are difficult to assess. It is unlikely that the small difference in average household size vitiates the results, because the full range of household sizes is represented in the sample. The relatively smaller number of subjects in the 45- to 54-year-old group could serve only to weaken the associations observed, because they are a group with high prevalence of chronic bronchitis (12).

The present study demonstrates a tendency for chronic bronchitis to cluster within households. Because we have confined the analysis to parents and their children, familial aggregation can be inferred. Fifty-seven per cent of the children reported on their own behalf. In the 43 per cent who were less than 12 years of age, for whom parents answered the questionnaire, only 2 cases of chronic bronchitis were observed, making it unlikely that the results were biased by parent over-reporting.

Moreover, the level of FEV$_1$ was found to have a greater similarity among members of a given household than among persons from different households (table 2). This similarity was observed among siblings (tables 2 and 3), between female children and their parents (table 4), but not between male children and their

parents. The observed difference in correlation between male and female children and their parents cannot be attributed to differences in age or to differences in smoking history (13) (table 6) between male and female children. The intraclass correlations found for siblings, although of a relatively small magnitude, were similar to those found in the Tecumseh study (4) for mixed male-female sibships less than 40 years of age (r, 0.17 to 0.25 for their FEV$_1$ score). The correlation coefficients for parent-child FEV$_1$ per cent predicted in table 4 are also similar to those for FEV$_1$ score found in the Tecumseh population. In that population, female children 10 to 39 years of age also showed a stronger correlation with maternal FEV$_1$ score than did male children, but this was not observed for fathers' or midparents' scores.

Maternal smoking history, measured as total number of cigarettes consumed, may have a significant adverse effect on FEV$_1$ per cent predicted in their male children (table 6). This effect was significant, even after the smoking history of the male children was accounted for in the analysis. The association of maternal FEV$_1$ per cent predicted and child's FEV$_1$ per cent predicted was no longer significant when either maternal or child smoking history was included in the analysis (table 5). This was largely due to the significant inverse correlation for maternal lifetime cigarette consumption and male child FEV$_1$ per cent predicted. The maternal FEV$_1$ per cent predicted was significantly associated with that of the children only in the regression that omitted both smoking histories (r = 0.15; P < 0.05). These effects of smoking were not found for fathers, although the mother-child and father-child regression coefficients for FEV$_1$ per cent predicted were not significantly different (r = 0.15 and 0.25, respectively; P > 0.2). The

ILDREN'S 1-SEC FORCED
PER CENT PREDICTED,
RETTE-SMOKING HABITS

		Standard Error of Estimate	Coefficient of Determination	F Value for Regression
ld ing - ary	Constant			
D†	107.77	11.75	0.22	4.97**
a†	102.40	16.47	0.11	2.47†

† excluded in the stepwise regression.

The observed difference in correlation male and female children and their parent be attributed to differences in age -rences in smoking history (13) (table n male and female children. The in-rrelations found for siblings, although rely small magnitude, were similar to ed in the Tecumseh study (4) for le-female sibships less than 40 years of 17 to 0.23 for their FEV$_1$ score). The a coefficients for parent-child FEV$_1$ per ted in table 4 are also similar to those score found in the Tecumseh population, female children 10 to f age also showed a stronger correla--maternal FEV$_1$ score than did male -ut this was not observed for fathers' ots' scores.

l smoking history, measured as total -cigarettes consumed, may have a sig-rerse effect on FEV$_1$ per cent predict-male children (table 6). This effect ant, even after the smoking history children was accounted for; in the se association of maternal FEV$_1$ per ted and child's FEV$_1$ per cent pre- o longer significant when either ma-uild smoking history was included in (table 5). This was largely due to unt inverse correlation for maternal arette consumption and male child at predicted. The maternal FEV$_1$ per ed was significantly associated with children only in the regression that h smoking histories (r = 0.15; P < effects of smoking were not found although the mother-child and fa--gression coefficients for FEV$_1$ per ed were not significantly different d 0.25, respectively; P > 0.2). The

reason for this sex difference in the effect of parental smoking history on child's FEV$_1$ per cent predicted is not apparent. Because not all of the households included in this analysis contained both parents, somewhat different subsets of children were used for the mother-child and the father-child comparisons; however, no differences between the 2 sets of subjects could be found in age, the proportion of smokers, or the proportion of male subjects. Data previously reported (15) showed that in this population, men and women who smoked or had smoked cigarettes showed no differences in the amount and duration of smoking, making it unlikely that mother-father differences in cigarette use accounted for the difference observed. The similarity of the regression coefficients for "child's smoking history" in table 6 suggests that smoking history was not a confounding element in this analysis.

The factors that underlie observed aggregation of FEV$_1$ remain, for the most part, undefined. The similarities between the correlation coefficients obtained for height and those obtained for FEV$_1$ per cent predicted suggest that the aggregation of FEV$_1$ may be largely a result of familial similarities in physical stature; however, use of FEV$_1$ per cent predicted and FEV$_1$ score in effect standardized the FEV$_1$ for height and age, making body physique an unlikely sole contributor to the observed aggregation. Despite recent work showing an increased susceptibility of persons with possibly the MZ and certainly the ZZ α_1-antitrypsin phenotype to obstructive airway disease (14–17), both phenotypes are of sufficiently low prevalence that their contribution to this aggregation is undoubtedly minimal (18). The possibility of other genetically determined liabilities to chronic bronchitis remains largely unexplored, except for twin studies (3) and isolated reports (4, 19).

The aggregation of FEV$_1$ and chronic bronchitis observed in this study may reflect, in large part, smoking patterns in the study households. The data presented in tables 5 and 6 concerning the effect of maternal and child smoking habits in modifying the correlation of maternal and child FEV$_1$ per cent predicted support a major role for cigarette smoking; however, the paternal FEV$_1$ predicted remains a significant predictor of female child's FEV$_1$ per cent predicted, independent of smoking effects.

The present study has demonstrated familial aggregation of both chronic bronchitis and level of pulmonary function in an urban popula-

tion; however, this and other studies (1–5, 19) leave unanswered many questions regarding the factors underlying familial aggregation of chronic bronchitis and FEV$_1$ and their role in determining susceptibility to obstructive airway disease. Prospective studies are currently in progress to define better this familial aggregation and its implications for obstructive airway disease.

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Schilling, R.S.F., Letai, A.D., Hui, S.L., Beck, G.J., Schoenberg, J.B., Bouhuys, A. "Lung Function, Respiratory Disease, And Smoking In Families" American Journal of Epidemiology 106(4): 274-283, 1977.

SUMMARY: Respiratory symptoms, disease and lung function were studied in 376 families with 816 children who participated in a survey in three USA towns. Parental smoking had no effect on children's symptoms and lung function. Also, there was no evidence that passive smoking affected either lung function or symptoms of adults. There was no association between prevalence of self-reported cough and/or phlegm in parents and their children. There was a highly significant association between the prevalence of wheeze in parents and their younger children, for whom parents reported this symptom. Wheeze in children was also significantly associated with a parental history of asthma, and lung function was lower in children with a family history of asthma. Even after accounting for height, weight, age, sex and race, children's lung function correlated significantly with parents' lung function. However, the contribution of familial factors (i.e., parents' lung function, smoking, and history of asthma) to children's lung function is small compared to the effects of height, weight and age.

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LUNG FUNCTION, RESPIRATORY DISEASE, AND SMOKING IN FAMILIES[1,2]

R.S.F. SCHILLING, A.D. LETAI, S.L. HUI, G.J. BECK, J.B. SCHOENBERG AND A. BOUHUYS

Schilling, R. S. F., A. D. Letai, S. L. Hui, G. J. Beck, J. B. Schoenberg and A. Bouhuys (Yale U. Lung Research Center, New Haven, CT 06510). Lung function, respiratory disease, and smoking in families. Am J Epidemiol 106: 274–283, 1977.

Respiratory symptoms, disease and lung function were studied in 376 families with 816 children who participated in a survey in three USA towns. Parental smoking had no effect on children's symptoms and lung function. Also, there was no evidence that passive smoking affected either lung function or symptoms of adults. There was no association between prevalence of self-reported cough and/or phlegm in parents and their children. There was a highly significant association between the prevalence of wheeze in parents and their younger children, for whom parents reported this symptom. Wheeze in children was also significantly associated with a parental history of asthma, and lung function was lower in children with a family history of asthma. Even after accounting for height, weight, age, sex and race, children's lung function correlated significantly with parents' lung function. However, the contribution of familial factors (i.e., parents' lung function, smoking, and history of asthma) to children's lung function is small compared to the effects of height, weight and age.

asthma; family characteristics; lung volume measurements; smoking

We investigated the contribution of familial factors, including smoking by parents, to lung function and respiratory symptoms in children. The study is a part of a population study in three towns in the United States in which members of families were questioned about respiratory symptoms and disease. Subjects were also given lung function tests measuring forced vital capacity (FVC), one second forced expiratory volume ($FEV_{1.0}$), peak expiratory flow rate (PEF) and maximum expiratory flow at 50 per cent of FVC (MEF50%) and at 25 per cent of FVC (MEF25%).

Children of smoking parents may suffer unduly from respiratory disease. For example, infants of mothers who smoke have significantly more attacks of bronchitis and pneumonia than infants of nonsmoking mothers (1). Also, children of smoking parents who may or may not have symptoms themselves have more bronchitis and pneumonia during their first year of life than children of nonsmoking parents (2), but this was not true during four subsequent years of follow-up. Nevertheless, older children may have an increased incidence of acute respiratory disease in homes where cigarettes are smoked (3, 4). These studies have led to the conclusion

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.... Nevertheless,
...n increased inci-
...ory disease in
...re smoked (3, 4).
...the conclusion

that passive smoking (inhaling other people's smoke) is injurious to health, particularly that of children (5).

The prevalence of cough in children however, is not only associated with parental smoking, but also with respiratory symptoms among parents (6, 7). After adjustment for the positive correlation between symptoms in parents and children, parental smoking had no significant effect on children's symptoms. Thus, smoking parents may affect their offspring's respiratory system indirectly, rather than via a direct effect of smoke. For example, smoking adults often cough and produce phlegm and thereby transmit infection (6).

All these results are based on children's symptoms as described by their parents. This may introduce bias. Parents who smoke have more symptoms and may be more conscious of them in their children. Parents who over- or under-report their own symptoms may do the same for their children. In this study, we have asked the children themselves some of the questions on respiratory symptoms. Also, children of smoking parents are more likely to smoke than children of nonsmokers (8). Unlike the previous studies, we have considered smoking habits of children in our analyses.

Familial resemblance in lung function, apart from the known factors of height, sex and ethnic group, appears to be slight, according to studies in twin pairs (9). Peak flow in five-year-old children correlates with peak flow in their parents (10), but this may be due to correlation between their heights. Peak flow in children was significantly related to their own histories of bronchitis and pneumonia, but there was no association between their peak flow and their parents' smoking habits, respiratory morbidity and social class. In the Tecumseh study (8), age- and height-adjusted $FEV_{1.0}$ scores correlated significantly not only between parents and their children, but also between siblings and even between spouses. However, these re-

sults were not controlled for smoking habits, nor were the possible effects of passive smoking on lung function considered. In the present study we have attempted to separate the effects of smoking from other familial factors on both lung function and respiratory symptoms.

MATERIALS AND METHODS

This investigation was part of a large survey on lung disease in the three towns of Lebanon and Ansonia in Connecticut, and Winnsboro in South Carolina. Families in which both parents and at least one child between the ages of seven and 18 had been examined were identified by name, address and telephone number. Family groups were checked from replies by parents about the numbers and names of their children and replies by children about their brothers and sisters, to eliminate those in which there was any doubt about the accuracy of the family grouping. There were 418 families with data for both parents and 915 children. We only report on the 376 white families since there were too few blacks for detailed analysis. Table 1 shows the distribution of the white families by town and by age and sex of the children.

The methods used for interviewing subjects and for measuring lung function have been described elsewhere (11). Prediction equations for lung function in white males and females were derived from the data of all healthy, lifetime nonsmoking adults and children in the total survey population (12). From these equations, the proportion (R^2) of the total variance in lung function

TABLE 1
Distribution of families by town and by age and sex of children

	Lebanon	Ansonia	Winns-boro	Total
Families	247	54	75	376
Boys 7-17	244	50	59	353
Boys 18+	35	8	14	57
Girls 7-14	188	41	48	277
Girls 15+	83	18	28	129

which is explained by height, weight, and age is determined.

The prediction equations were derived separately for boys aged 7-17 and men aged 18+, and for girls aged 7-14 and women aged 15+ (12). Since there were few older children, only the girls aged 7-14 and boys aged 7-17 (the age ranges in the prediction equations for children) were included in the present analysis of lung function. Residual lung function was obtained for each subject by subtracting the predicted value from the observed value. A residual of less than zero means that lung function is lower than expected from the data in healthy lifetime nonsmokers. Since the prediction equations for girls and boys use the natural logarithm (ln) of the function values, the residuals of children are obtained in transformed units (e.g., residual ln FVC); values for men and women are expressed in liters or liters/sec.

Symptoms and chest illnesses were defined as follows:

Cough and/or phlegm—usual cough at any time of the day or night, and/or usual phlegm production at any time of the day or night.

Wheeze—any history of wheezing or chest tightness.

Asthma—"yes" to the question, "Have you ever had bronchial asthma?"

Bronchitis—"yes" to the question, "Have you ever had bronchitis?"

Pneumonia—"yes" to the question, "Have you ever had pneumonia?"

Family history of asthma—"yes" to the question, "Have your parents, brothers, sisters, or children ever had asthma?"

All subjects including children answered the questions on smoking, cough and phlegm for themselves. Parents answered the questions on wheeze and on family history of asthma for children aged 15 and under. Data on chest illnesses in children were not analyzed because some of the answers were thought to be unreliable.

To relate the socioeconomic class of parents to the symptoms and lung function of their children, we classified fathers into eight groups based on the US Department of Labor's occupational classification of 1965 (13), and mothers as either housewives or those working outside their homes.

RESULTS

Symptoms. We determined the prevalence of symptoms in groups according to symptom prevalence in parents: 1) neither parent had the symptom, 2) mother only had the symptom, 3) father only had the symptom, or 4) both parents had the symptom. Prevalences of cough and/or phlegm were highest in children in group 4, but there was no association between parents' and children's symptoms when all four groups were compared (table 2). The results were the same for children who had never smoked. For wheeze, the prevalence in parents correlated significantly with that in their children aged 15 years and under, but not with prevalence in older children, possibly because of smaller numbers (table 3). However, parents answered the wheeze questions for the younger children; only the older ones answered for themselves. Again, the results were similar in the subsample of children who had never smoked.

The association between parents' smok-

TABLE 2

Prevalence of cough and/or phlegm in children by cough and/or phlegm in their parents

Parents' cough phlegm	All boys		All girls	
	Total	Cough phlegm No. (%)	Total	Cough phlegm No. (%)
Neither	221	32 (14)	218	24 (11)
Mother	50	7 (14)	35	5 (14)
Father	113	19 (17)	105	10 (9)
Both	26	7 (27)	48	9 (19)
x^2	2.91		3.06	
P	0.41		0.38	

ing and children's symptoms was examined by comparing a group in which parents were both present nonsmokers with a group in which at least one parent was a present cigarette smoker. There were no significant differences between these groups in the prevalence of either cough and/or phlegm or wheeze in either boys or girls. When the nonsmokers were further divided into either ex-smokers or lifetime nonsmokers, the results remained insignificant. Also, there was no significant interaction between parent's symptoms and smoking in relation to children's symptoms.

Although no association was found in the prevalence of cough and/or phlegm between mothers and fathers, there was a significant relationship in the prevalence of wheeze ($x^2 = 6.44; p < 0.025$). Symptoms in parents were related to their smoking habits. Cough, phlegm and wheeze were significantly more prevalent among male and female current smokers. However, prevalence of these symptoms in nonsmokers was unrelated to whether or not their spouses smoked.

We also attempted to relate symptom prevalences in children to their parents' reports of respiratory illness. Families were classified into non-mutually exclusive groups in which at least one parent ever had 1) bronchitis, 2) pneumonia, or 3) asthma. Each of these groups was compared to a group in which neither parent ever had any of these illnesses. There were no significant differences in the proportion of children with cough and/or phlegm in each parent-illness group, compared to the no-illness group. A significantly higher proportion of girls reported wheeze in the parents' asthma group; this was also true for boys in all three parent illness groups (table 4). Symptom prevalences in children were similar among socioeconomic classes as defined by father's occupation. We also compared four groups defined by the mother's work and current smoking status (nonsmoking or smoking; housewife or working). Here, the only significant finding

TABLE 3

Prevalence of wheeze in children by age and by wheeze in their parents

Parents' wheeze	Total	Wheeze No (%)	Total	Wheeze No (%)
		Boys 7-15		Boys 16+
Neither	154	22 (14)	66	10 (15)
Mother	44	10 (23)	23	4 (17)
Father	72	9 (13)	15	4 (27)
Both	29	13 (45)	7	3 (43)
x^2	17.67		3.85	
P	<.001		0.28	
		Girls 7-15		Girls 16+
Neither	172	16 (9)	59	9 (15)
Mother	49	10 (20)	16	4 (25)
Father	54	7 (13)	16	1 (6)
Both	33	10 (30)	7	0 (0)
x^2	12.18		3.56	
P	<.01		0.31	

TABLE 4

Prevalence of wheeze in children in relation to chest illnesses in their parent(s)

Parent(s)	All boys			All girls		
	Total	Wheeze No (%)	x^2	Total	Wheeze No (%)	x^2
No illness	161	17 (11)		170	19 (11)	
Bronchitis	137	36 (26)	11.45†	125	22 (18)	1.98
Pneumonia	173	35 (20)	5.22*	182	30 (16)	1.65
Asthma	41	14 (34)	12.24†	48	17 (35)	14.24†

* $p < .025$.
† $p < .001$ for comparisons between symptom prevalence in parent-illness group and parent no-illness group.

was that daughters of smoking working women reported more wheeze than daughters of the other three groups ($x^2 = 10.5$; $p < 0.025$).

Lung function. To examine both active and passive smoking in relation to lung function in parents, we divided the families into four groups according to parents' current cigarette smoking: 1) both smokers, 2) father smoker, mother nonsmoker, 3) mother smoker, father nonsmoker, 4) both nonsmokers. Forty-six families in which one parent smoked only pipes or cigars were excluded because the numbers were too small. The results of an analysis of variance for residual $FEV_{1.0}$ in the four groups are shown in table 5. The highly significant differences in the mean residuals indicate the expected adverse effect of active smoking with one exception: the men in the group where only their wives smoked also had low residuals. These men were further subdivided by their past smoking history. The men who never smoked themselves (but whose wives smoked) did not deviate significantly from normal; the male ex-smokers in the group had particularly low lung function. In the families in which only the father smoked, the mother's lung function was similar to that in which neither parent smoked. Thus, passive smoking was not an important factor affecting adult lung function.

To determine the effect of passive smoking on lung function in children, we used analysis of variance to compare lung function residuals of boys aged 7-17 or girls aged 7-14, divided according to the four parent smoking categories. Girls' MEF50% and MEF25% were lowest in those families in which only the mothers smoked, but differences were not significant. When the analysis was repeated for the subsample of children who had never smoked themselves, this difference for MEF50% was significant ($F = 2.65$; $p < 0.05$).

Residual lung function in children was also studied in relation to their parents' history of chest illness. Boys aged 7-17 and girls aged 7-14 were classified into parent-illness groups, as for the symptom analysis. For the asthma group, the five mean residuals were lower in both boys and girls than in the parent no-illness group. These differences were significant for $FEV_{1.0}$ ($t = 2.08$; $p < 0.05$) and PEF ($t = 3.51$; $p < 0.001$) in girls. The trend toward lower function residuals in children of parents with bronchitis or pneumonia was not significant.

From parents' answers to the questions on family history of asthma, we obtained information on the children's first and second degree relatives. All mean residuals were lower in the children who had at least one relative with asthma, compared to children who had none; results were significant for $FEV_{1.0}$, MEF50%, and MEF25% in boys (table 6).

There was no significant relation between family socioeconomic status and

TABLE 5

Mean residual $FEV_{1.0}$* of parents by current smoking category (n = no. of pairs)

		Residual $FEV_{1.0}$, liters				
		Both smokers (n = 75)	Father smoker, mother nonsmoker (n = 74)	Mother smoker, father nonsmoker (n = 40)	Both nonsmokers (n = 136)	F
Fathers,	x̄	-0.42	-0.35	-0.24	-0.06	11.66†
	(SEM)‡	(0.05)	(0.06)	(0.07)	(0.04)	
Mothers,	x̄	-0.24	0.00	-0.13	-0.09	5.66*
	(SEM)	(0.04)	(0.04)	(0.07)	(0.03)	

* The results for residual FVC and flow rates show similar trends.
† $p < .01$.
‡ Standard error of mean.

TABLE 6

Residual lung function in children in relation to family history of asthma*

		Boys 7-17			Girls 7-14		
		Family asthma (n = 158)	No family asthma (n = 195)	t	Family asthma (n = 119)	No family asthma (n = 158)	t
Residual FEV$_{1.0}$	$\bar{x}$	-0.035	-0.002	2.57†	-0.020	0.004	1.85
	(SEM)	(0.009)	(0.009)		(0.010)	(0.009)	
Residual MEF50%	$\bar{x}$	-0.044	0.001	2.64‡	-0.020	-0.010	0.56
	(SEM)	(0.012)	(0.011)		(0.013)	(0.011)	
Residual MEF25%	$\bar{x}$	-0.055	0.000	2.85‡	-0.028	-0.017	0.54
	(SEM)	(0.013)	(0.014)		(0.015)	(0.013)	

* All children's lung function residuals are expressed on the natural logarithm scale, and not as liters or liters/sec.

† $p < 0.05$.

‡ $p < 0.01$.

TABLE 7

Correlations between residual lung function in spouses and in parent-child pairs (n = no. of pairs)

	Spouses (n = 376)	Father-son age 7-17‡ (n = 353)	Father-daughter age 7-14 (n = 277)	Mother-son age 7-17 (n = 353)	Mother-daughter age 7-14 (n = 277)
Residual FVC	.07	.19†	.21†	.15†	.12*
Residual FEV$_{1.0}$	.07	.17†	.23†	.11*	.16*
Residual PEF	.10	.19†	.20†	-.01	.06
Residual MEF50%	.07	.20†	.15*	.17†	.12*
Residual MEF25%	.07	.13*	.03	.26†	.09

* $p < .05$.

† $p < .01$.

‡ Age of child.

mean lung function residuals of sons or daughters of fathers from the various occupational groups. Also, there were no differences in children's residuals among the four groups defined according to mothers' work and smoking status (housewife or working; nonsmoking or smoking).

A comparison of lung function residuals between groups eliminates the effects of height, weight and age (12). Thus, any correlation between residuals of spouses, parents and children, or of siblings would suggest an effect of other factors, such as family resemblance in lung function (tables 7 and 8). Analysis of covariance showed that lung function residuals of children in the four parent smoking groups (both smokers; father smoker, mother nonsmoker; mother smoker, father nonsmoker; both nonsmokers) were the same after adjusting for mothers' and fa-

thers' residuals. Hence, the different smoking groups may be combined for the analysis of parent-child correlations. In these correlations, each parent-child pair was counted independently; i.e., if a father had three sons, he was included three times, once with each son, in the father-son correlation. For the sibling correlations, the oldest sib was paired with the sib closest to him in age. Then the second oldest was paired with the third oldest and so on. Thus each sib except the oldest and youngest was a member of two pairs, once as the older and once as the youngest of the pair. None of the correlation coefficients between spouses were significant. In other pairs, at least three out of the five residuals yielded significant results, except between brothers. For children who had never smoked, the correlations were similar to those in all children shown in

Table 8

Correlations between residual lung function in siblings (n = no. of pairs)

	Brothers age 7-17 (n = 103)	Sisters age 7-16 (n = 65)	Opposite-sex sibs. (n = 214)	All sibs (n = 382)
Residual FVC	.15	.33†	.32†	.27†
Residual FEV$_{1.0}$	.12	.26*	.25†	.21†
Residual PEF	-.02	.26*	.16*	.12*
Residual MEF50%	.19	.09	.17*	.16*
Residual MEF25%	.04	.22	.13	.12*

* $p < .05$.
† $p < .01$.

tables 7 and 8. Positive correlations between parents' and children's lung function residuals persisted when families with histories of asthma in parents or relatives were excluded.

The contribution of familial factors and passive smoking to children's lung function can be assessed from a multiple regression analysis (table 9). The child's lung function measurement (not the residual) was the dependent variable. The independent variables were the height, weight, and age terms from the original prediction equation (12), and the parents' lung function residuals, the four parents' smoking categories, and a family history of asthma. Mothers' or fathers' residuals, or both, were significant variables for several measurements in boys as well as girls. The variable representing families in which the mother smokes was significant for MEF50% in girls. For girls aged 10 years, of average height and weight (148 cm, 32 kg), the predicted MEF50% was 2.86 liters/sec if the mother smoked, and 3.05 liters/sec if she did not. The family history of asthma variable was significant for boys' FEV$_{1.0}$ and MEF25%. Quantitatively, this variable, too, caused only a small difference in predicted values (e.g., at age 10, height 148 cm, weight 40 kg, FEV$_{1.0}$ for boys with a family history of asthma was 2.19 liters, versus 2.25 liters for those without). When only children who had never smoked were included in the analysis, the results were similar, except that the family history of asthma var-

iable was also significant for boys' MEF50%.

Table 9 also shows the percentage of the variance (R^2) in the children's lung function measurements which is explained by the height, weight and age terms, and by the addition of the significant family terms. The greatest proportion of the variance is explained by the height, weight, and age terms (R^2_1). Relatively little is added by the parents' residuals, the smoking term, or the asthma term (compare R_1 with R^2_2).

DISCUSSION

We have found no significant relation between parents' smoking and respiratory symptoms or lung function in their children. Previous reports that "passive smoking" may cause respiratory disease in children (1, 3, 4) were based on symptoms only. They did not exclude the possibility that the effect of passive smoking may be indirect, by transmission of infection from coughing parents to their children. In two studies (6, 7), the association between parental smoking and symptoms could be attributed to increased cough or phlegm among smoking parents. In only one study (2), infant respiratory disease was associated with parental smoking, even if the parents had no symptoms, but this association was absent in children aged 1-5.

In relating parents' and children's symptoms, bias may be introduced when parents answer the questions for their offspring. In our study, all children them-

TABLE 9

Contribution of parents' residual lung function and smoking habits and family history of asthma to children's lung function

Lung function	R^2* (%)	R^2† (%)	Significant parent terms			
			Mothers' residual	Fathers' residual	Only mother smokes‡	Family asthma
Boys (n = 353)						
FVC	90.2	90.7	$p < .01$	$p < .01$		
FEV$_{1.0}$	89.8	90.3		$p < .01$		$p < .05$
PEF	80.6	81.2		$p < .01$		
MEF50%	68.7	70.8	$p < .01$	$p < .01$		
MEF25%	54.4	58.2	$p < .01$			$p < .05$
Girls (n = 277)						
FVC	86.2	87.1	$p < .05$	$p < .01$		
FEV$_{1.0}$	86.5	87.7	$p < .01$	$p < .01$		
PEF	66.4	67.8		$p < .01$		
MEF50%	53.1	54.8		$p < .01$	$p < .05$	
MEF25%	37.4	37.4				

* R^2 is the percentage of the variance in children's lung function which is explained by regression on height, weight and age terms.

† R^2 is the percentage of the variance in children's lung function which is explained by regression on height, weight, and age terms and on significant parents' residuals, parents' smoking category terms, and family history of asthma term.

‡ Variable reflecting families in which the mother smokes but the father does not. Variables which were never significant reflected other family smoking categories (neither parent smokes, only father smokes, both parents smoke).

selves answered questions about cough and phlegm; there was no significant association between the prevalence of those symptoms in parents and children (table 2). Nor did the children of parents with cough and phlegm have significantly lower lung function. The association between cough and phlegm in parents and children in other studies may result from bias due to parents answering the children's questions.

For wheezing, parents answered the questions for children aged 15 and under, but not for older children. The prevalence of wheeze in parents correlated with that in younger children, but not with wheeze in older children. To test the reliability of parents' reports on their children's wheeze, residual lung function of the younger children was examined. For boys the results follow the same pattern as the symptom analysis, with significantly lower residuals in children whose mother or both of whose parents wheeze than in children whose parents do not wheeze (for

FEV$_{1.0}$, PEF and MEF50%, $p < 0.01$). However, no differences were observed in the girls. Thus, the association between wheeze in parents and children may be real, at least in boys.

The significant correlations between lung function residuals of parents and their children indicate familial resemblances in lung function which are not due to inherited similarities in height and weight nor to a family history of asthma. In the Tecumseh study (8), Higgins and Keller found significant correlations between family members in their height- and age-adjusted FEV$_{1.0}$ scores. The present study confirms these findings and extends them to other lung function measurements as well.

However, we did not find the small but significant correlations which Higgins and Keller showed between spouses (table 7). This might be because the number of spouses in Tecumseh (1770 pairs) is larger than ours (376 pairs). Secondly, many of the husbands and wives in our study were

not examined at the same time; in Tecumseh, spouses were usually seen together, and thus calibration and other factors (e.g., acute respiratory illness in family) might yield slightly higher correlations. In addition, we found no significant correlations between brothers aged 7-17, although there were significant correlations between sisters 7-14 and in brother-sister pairs. Excluding boys aged 15-17, thus making the age grouping comparable to that for girls, does not change the results for brother pairs. Nor are the results different when boys who have smoked cigarettes are excluded. The lack of a significant correlation in brothers is difficult to explain.

After accounting for height, weight, age, sex and race, the additional contribution to children's lung function from the parents, although significant, is relatively small (table 9). It could easily be missed when smaller numbers are studied (9). The largest relative increase of R^2 occurs for MEF25% in boys, where the height, weight and age terms explain 54.5 per cent of the variance; the other family factors add a further 3.8 per cent. Even here, the effect on the absolute value of lung function is small. Predicted MEF25% for 11-year-old boys (height 161 cm, weight 45 kg) is 1.62 liters/sec if only height, weight and age are considered. Adding the average mothers' residual decreases this value to 1.60 liters/sec, and further addition of the family history of asthma variable decreases MEF25% to 1.48 liters/sec. Thus familial factors, apart from those related to height, weight, age, sex and race, are relatively unimportant in determining lung function.

Chronic obstructive lung disease and even more, asthma, may in part be determined genetically (14-16). Children with a family history of asthma have lower residuals for all lung function measurements than children without such a history (table 6). Girls show the same trends as boys but the differences are not so marked. Wheez-

ing in parents is associated with lower lung function residuals in boys but not in girls. Asthma may begin at an earlier age in boys than in girls (17, 18), and boys might be more exposed to antigenic agents in their work or hobbies. Both familial and environmental factors may contribute to reduction of lung function in children who have a family history of asthma or whose parents wheeze.

There have been no convincing reports on the influence of passive smoking on either adults' or children's lung function. In our study, as expected, adult smokers had much lower lung function residuals than the nonsmokers (table 5), but there was no evidence that exposure to one's spouse's cigarette smoke affected lung function. Nor do the results of this study suggest that parents' smoking has anything but a minor effect on children's lung function. The only significant finding was that daughters' flow rates were lowest in families in which the mother smoked and the father was a nonsmoker (table 9). This could be due to chance, and the effect is in any case small.

Heavy exposure to other people's smoke causes nonsmokers to absorb carbon monoxide and nicotine and sensitive individuals to develop cough, wheeze, and respiratory distress (19). People are, however, rarely if ever subjected to such extreme conditions in the home. Although an environmental study of 20 homes showed higher particulate levels in homes with smokers, there was no evidence that this was related to the presence or absence of disease in children (20). We conclude that exposure to low levels of smoke produced by cigarette smokers does not result in chronic respiratory symptoms or loss of lung function among children nor among adults.

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SUMMARY: Two hundred and fourteen children aged 7-11 years had tests of lung function performed. Mothers were asked about their past and current smoking habits and whether their children had ever had pneumonia or severe bronchitis. The findings suggest a relationship between early childhood bronchitis or pneumonia and impairment of lung function in later childhood and also suggest that maternal smoking habit may contribute directly to impairment of lung function in children.

RESPIRATORY ILLNESS, MATERNAL SMOKING HABIT AND LUNG FUNCTION IN CHILDREN

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Summary

Two hundred and fourteen children aged 7–11 years had tests of lung function performed. Mothers were asked about their past and current smoking habits and whether their children had ever had pneumonia or severe bronchitis. The findings suggest a relationship between early childhood bronchitis or pneumonia and impairment of lung function in later childhood and also suggest that maternal smoking habit may contribute directly to impairment of lung function in children.

INTRODUCTION

Previous studies (Lunn et al. 1967; Holland et al. 1969) have demonstrated a relationship between bronchitis and pneumonia in early childhood and impairment of lung function in later life. Other work (Colley et al. 1974) has shown that parental smoking can contribute to the development of respiratory illness in early childhood. The present paper explores the influence of these features on subsequent lung function in children.

Methods

In the course of a community study of respiratory function in relation to housing conditions 214 children aged 7–11 years were seen at school. Each child's lung function was measured by the use of a bellows spirometer; heights and weights were recorded. Each child's mother was interviewed at her home.

All lung function measurements were made during the summer months. The following lung function indices were calculated for each child from the spirometer tracings: the forced mid-expiratory flow (FMF); the forced expiratory volume in 0.75 of a second ($FEV_{0.75}$); the forced vital capacity (FVC). Statistical methods have been described in detail previously (Yarnell & St Leger 1977) but are summarized briefly below.

The lung function measurements were converted to height-standardized indices by use of the relationship: Derived index $= LFT/Height^K$, where LFT is the spirometric result for each index of lung function and for each child; the exponent K is a constant for each lung function index and for each sex. Values of K were calculated from pooled data from this study and are shown in Table 1.

The values of the derived indices have been re-standardized to a height of 130 cm to facilitate comparison of results.

Table I. Values of exponent *K* estimated from pooled data

Lung function test	Males	Females
FMF	2.05	2.54
$FEV_{0.75}$	2.20	2.04
FVC	2.20	1.89

Results

Fig. 1 shows the mean values of the lung function indices standardized to a height of 130 cm, according to the presence or absence of a history of bronchitis or pneumonia in each child. Children with a history of bronchitis or pneumonia have, on average, lower values for the lung function indices FMF and $FEV_{0.75}$ compared to children without such a history. Average FVC values are reduced to a lesser extent. The average reduction in FMF for boys is 9%; and for girls is 12%; the average reduction in $FEV_{0.75}$ for boys is 5%; and for girls is 7%.
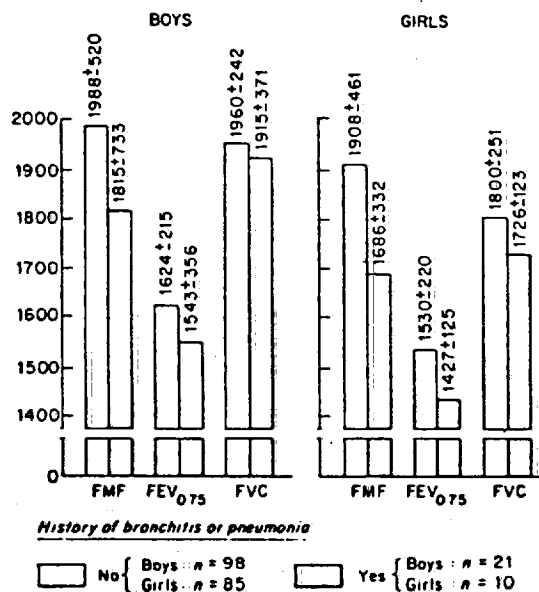
Fig. 1. Lung function and past history of chest infection (mean ± sd) standardized to height of 130 cm (FMF ml/sec; $FEV_{0.75}$ ml; FVC ml)

Table II shows the distribution of children with and without a history of bronchitis or pneumonia according to the smoking habit of their mothers in pregnancy. Fig. 2 shows that the offspring of mothers who reported that they had smoked more than 10 cigarettes daily throughout pregnancy had reduced lung function (FMF and $FEV_{0.75}$) compared
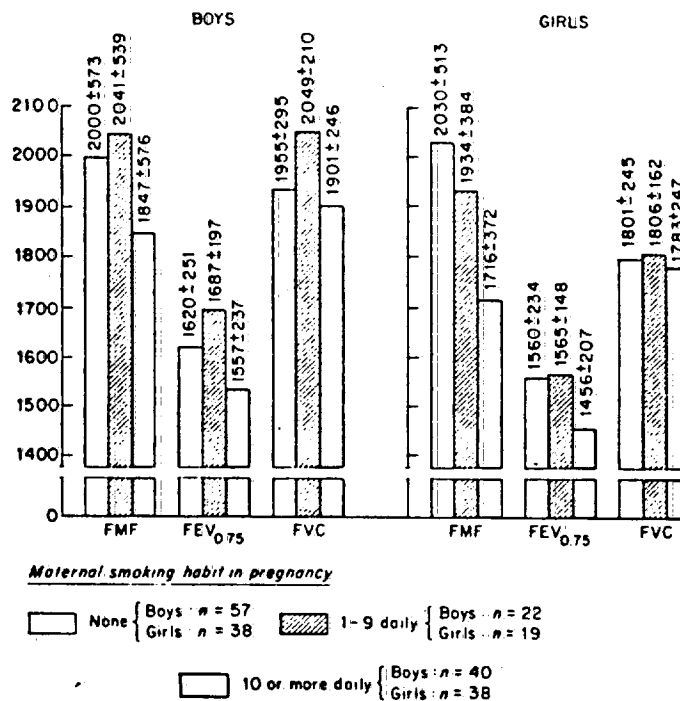
Fig. 2. Lung function and maternal smoking habit in pregnancy (mean ± SD) standardized to height of 130 cm (FMF ml/sec; $FEV_{0.75}$ ml; FVC ml)

Table II. Numbers of children with history of bronchitis or pneumonia by maternal smoking habit in pregnancy

Maternal smoking habit in pregnancy	Boys		Girls	
	No history	Bronchitis or pneumonia	No history	Bronchitis or pneumonia
None	49	8	34	4
1-9 daily	18	4	15	4
10 or more daily*	31	9	36	2
Total	98	21	85	10

* Very few mothers reported having smoked 20 or more cigarettes daily throughout pregnancy
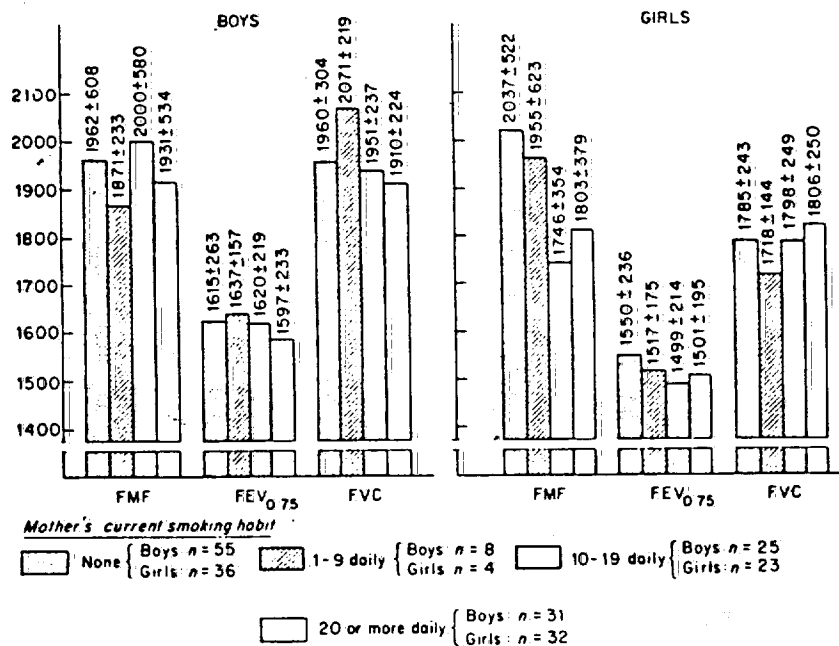
Fig. 3. Lung function and mother's current smoking habit (mean ± SD) standardized to height of 130 cm (FMF ml/sec; FEV$_{0.75}$ ml; FVC ml)

function of their children is examined no consistent trends are shown. Although a reduction in FMF and FEV$_{0.75}$ in the female offspring of mothers who currently smoke 20 or more cigarettes daily is apparent.

Table III shows the children's lung function in relation to the mother's smoking habit during pregnancy and the current household smoking habit (this includes an estimate of the number of cigarettes currently smoked within the home by other household members – usually the father– in addition to the mother's own consumption). This analysis fails to show any further reduction in the lung function of children with increasing household cigarette consumption.

DISCUSSION

The present findings support the evidence for a relationship between early childhood bronchitis or pneumonia and subsequent impairment of lung function in children. Five of the mothers whose children had had bronchitis or pneumonia also said that their child had had asthma at some stage during the child's life. Since the majority of these children had lung function values which were close to the average values for each height group, this subgroup of children did not contribute significantly to the trends shown in Fig. 1.

In the present study the impairment of lung function of children whose mothers smoked more than 20 cigarettes throughout pregnancy did not appear to be wholly

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Table III. Lung function indices (mean, standardized to height of 130 cm) by maternal smoking habit during pregnancy and current household smoking habit (number of subjects shown in parentheses)

Lung function test	Household smoking habit	Boys Maternal smoking in pregnancy			Girls Maternal smoking in pregnancy		
		None	1-9 daily	10 or more daily	None	1-9 daily	10 or more daily
FMF (ml/sec)	None	1988 (18)			2088 (9)	2409 (1)	
	1-9 daily	1996 (15)	2095 (3)	1934 (2)	1770 (12)	2348 (2)	1346 (1)
	10-19 daily	1951 (17)	2102 (8)	1778 (12)	2264 (12)	1819 (9)	1702 (12)
	20 or more daily	2160 (7)	1983 (11)	1873 (26)	1969 (5)	1894 (7)	1739 (25)
$FEV_{0.75}$ (ml)	None	1557 (18)			1587 (9)	1776 (1)	
	1-9 daily	1682 (15)	1843 (3)	1754 (2)	1472 (12)	1608 (2)	1445 (1)
	10-19 daily	1593 (17)	1637 (8)	1521 (12)	1606 (12)	1521 (9)	1435 (12)
	20 or more daily	1727 (7)	1678 (11)	1557 (26)	1622 (5)	1575 (7)	1466 (25)
FVC (ml)	None	1879 (18)			1781 (9)	2038 (1)	
	1-9 daily	2036 (15)	2344 (3)	2197 (2)	1751 (12)	1712 (2)	1946 (1)
	10-19 daily	1928 (17)	1923 (8)	1901 (12)	1817 (12)	1791 (9)	1734 (12)
	20 or more daily	2027 (7)	2058 (11)	1875 (26)	1916 (5)	1818 (7)	1791 (25)

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caused by an increased tendency to develop bronchitis or pneumonia in early childhood. A slightly greater proportion of boys whose mothers had smoked during pregnancy had a history of bronchitis or pneumonia compared to boys of mothers who had not smoked (Fig. 2), but this tendency is not apparent in girls.

A previous study by Colley et al. (1974) suggested that passive smoking by infants from parental cigarette consumption contributed towards the development of bronchitis or pneumonia in the first year of life. In the present study data on parental smoking habit during each child's first year of life are not available; current paternal smoking habit (recorded in total household smoking habit), however, which is unlikely to have altered substantially throughout the life of the child, does not contribute towards impairment of lung function in a child.

Respiratory morbidity in children varies with the social class of their families (Colley & Reid 1970). Fathers of children in the present study population were predominantly employed in manual and unskilled occupations; the social class of mothers who had smoked and those who had not smoked during pregnancy was therefore similar.

In a previous report on these data we showed that children's lung function differed in three areas of different housing (Yarnell & St Leger 1977). The relative impairment in lung function of children of mothers who smoked 10 or more cigarettes daily during pregnancy reported here is independent of the formerly reported association, however; this tendency is present in all areas of housing in girls and in all areas but one in boys.

In view of the known limitations of certain historical data (Hamman et al. 1975; Lunn et al. 1970), the present findings must be interpreted with some caution. They do suggest, however, that heavy smoking during pregnancy may have a direct effect on the offspring's subsequent lung function which persists at least into late childhood. As noted by Bland et al. (1974) mild impairment of lung function may not be of immediate clinical significance to individual children but may nevertheless indicate a predisposition to chronic bronchitis in adult life. This latent disposition would only be activated by additional factors in adult life; the most important of these is cigarette smoking.

Many studies have reported the long-term effects on the child of maternal smoking during pregnancy (reviewed by Rush & Kass 1972; Butler et al. 1972) but there are few reports of acute effects during pregnancy. Three such reports (Manning et al. 1975; Gennser et al. 1975; Manning & Feyerabend 1976) note that fetal breathing movements are inhibited by maternal cigarette smoking. If the findings of the present study are confirmed these reports may explain at least part of the impairment of lung function in children of mothers who smoked heavily during pregnancy of a mechanism which operates *in utero*.

ACKNOWLEDGEMENT

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Tager, I.B., Weiss, S.T., Rosner, B., Speizer, F.E. "Effect of
Parental Cigarette Smoking on the Pulmonary Function of Children"
American Journal of Epidemiology 110(1): 15-26, 1979.

SUMMARY: The authors have investigated the effects of parental
smoking patterns on the pulmonary function of children in East
Boston, Massachusetts. A crude inverse dose-response relationship
was observed between the level of FEF25-75% predicted of children
who never smoked and the number of smoking parents in the household.
Compared to children with two non-smoking parents, the level of
FEF25-75% predicted was 0.156 and 0.355 standard deviation units
lower for children with one and two currently smoking parents,
respectively. An additional decline in level of FEF25-75% predicted
was observed for children who themselves had smoked.   Smoking
children with two smoking parents had an average of FEF25-75%
predicted level which was 0.355 standard deviation units lower
than non-smoking children with two smoking parents. These data
not only confirm that cigarette smoking by young children and
teenagers has direct measurable effects on their pulmonary function,
but also show that cigarette smoking by parents has a measurable
effect on the pulmonary function of their children which is
independent of any direct use of cigarettes by the children.

EFFECT OF PARENTAL CIGARETTE SMOKING ON THE PULMONARY FUNCTION OF CHILDREN

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Tager, I. B. (Channing Laboratory, 180 Longwood Ave., Boston, MA 02115), S. T. Weiss, B. Rosner and F. E. Speizer. Effect of parental smoking on the pulmonary function of children. *Am J Epidemiol* 110:15–26, 1979.
The authors have investigated the effects of parental smoking patterns on the pulmonary function of children in East Boston, Massachusetts. A crude inverse dose-response relationship was observed between the level of $FEF_{25-75}\%$ predicted of children who never smoked and the number of smoking parents in the household. Compared to children with two non-smoking parents, the level of $FEF_{25-75}\%$ predicted was 0.156 and 0.355 standard deviation units lower for children with one and two currently smoking parents, respectively. An additional decline in level of $FEF_{25-75}\%$ predicted was observed for children who themselves had smoked. Smoking children with two smoking parents had an average $FEF_{25-75}\%$ predicted level which was 0.355 standard deviation units lower than non-smoking children with two smoking parents. These data not only confirm that cigarette smoking by young children and teenagers has direct measurable effects on their pulmonary function, but also show that cigarette smoking by parents has a measurable effect on the pulmonary function of their children which is independent of any direct use of cigarettes by the children.

respiratory tract infections; smoking

Despite the continued warnings concerning the health hazards of cigarette smoking, large numbers of adults continue to smoke cigarettes (1), and increasing numbers of teenagers have also taken up the practice (2). The continued use of cigarettes has raised concerns regarding the effect on non-smokers of breathing cigarette smoke. A number of studies (3) have documented that, depending on such factors as ventilation, the number of cigarettes smoked, and the volume of the enclosed space, cigarette smoking can impose a pollutant burden that may potentially be hazardous to the health of exposed non-smokers.

Other studies (4–11) have demonstrated that children who are exposed to parents who smoke carry an increased burden of respiratory illness. This association has been observed as early as the first year of life (7, 8, 10), and it has been noted to extend into the early teens (4, 6, 9). Both acute respiratory illness episodes (4–8, 10) as well as occurrence of chronic

symptoms (9, 11) have been reported. However, with the exception of a study by Schilling et al. (12) which failed to find any effect, the pulmonary function correlates of the exposure to parental smoking have been largely unexplored.

As part of a prospective study of risk factors for obstructive airways disease which may be operative early in life, we have investigated the effects of parents' smoking patterns on the pulmonary function of their children. Our findings suggest that a child's passive exposure to cigarette smoke has an adverse effect on the child's pulmonary function.

MATERIALS AND METHODS

Selection of the sample

A random sample was selected from all children, aged 5-9-years-of-age, in the public and parochial schools of East Boston, Massachusetts, as of September, 1974. Thirty-two per cent of all children in each school in the community studied were randomly chosen to ensure a uniform geographic distribution in the community. The number of children initially selected for this study was based on estimates of expected refusal rates and on the estimated number of children needed for a follow-up study on familial patterns of chronic productive cough symptoms and obstructive airways disease as determined from a previous study in this community (13). Table 1 details the outcome of the selected sample.

The community of East Boston is a geographically defined neighborhood within the city of Boston in which the inhabitants are of predominantly Italian-American descent. Sixty-three per cent of working adults in the present sample were employed as clerks (or in related clerical positions), craftsmen, service workers, or were among the operatives defined by the US Census definitions (14). Only 5 per cent held professional, technical or managerial positions. Approximately 40 per cent of the adults had at least a high school diploma.

Screening of the sample

Between January and June, 1975, interviewers visited the households of the children who had been selected for the random sample. These interviewers had been specially trained using materials provided by the Division of Lung Diseases, National Heart, Lung and Blood Institute (NHLBI). They enumerated all residents of the households and asked each to attend a special neighborhood clinic where we could obtain respiratory symptom and illness histories and measure of pulmonary function. Those families who agreed to participate but who did not come to the clinic were screened in their homes.

Standardized questionnaires were used to obtain histories of respiratory symptoms and illness as well as smoking histories and demographic data. Separate questionnaires were administered by the

TABLE 1

Outcome of sample of index children aged 5-9 years selected for study of the effect of parental smoking on their pulmonary function, East Boston, MA, 1974

Sample	No. of children
Selected	806
Not available*	116
Total living in study community	690
Not contacted after 3 home visits	50
Located	640
Parents refused	175 (27.3%)†
Language problem‡	5
Other	4
Total interviewed	456 (71.3%)†
Total with usable data	444 (69.4%)†

* The large proportion of persons who moved prior to being contacted can be attributed directly to a period of instability related to problems of school desegregation in the city of Boston.
† Per cent of 640.
‡ Did not speak English or Italian.

interviewers for subjects less than 10 years of age and those 10 years and older. Questions relating to chronic cough, phlegm and chest illness were those proposed for lung program epidemiology studies by the Division of Lung Diseases, NHLBI (15). Parents answered for children ages 10 years and younger for all questions except those pertaining to the child's smoking history; all other persons answered for themselves. Smoking histories were obtained from all children in the absence of their parents during the pulmonary function testing.

Pulmonary function testing

Subjects performed forced vital capacity (FVC) maneuvers while in the sitting position and without the use of a nose clip, using an eight liter, water-filled, portable, recording spirometer (Survey Spirometer, Warren Collins, Inc., Braintree, MA). Subjects were encouraged to perform FVC maneuvers until five acceptable tracings were obtained, or until it became evident that they could not perform adequately. A tracing was considered acceptable if it was at least four seconds in duration (adults were encouraged to blow for at least six seconds) and if the interviewer felt that a maximal effort had been made. All tests on children were done by one of two interviewers, each with at least two years of experience. Each subject's standing height was measured without shoes to the nearest one-half inch. All pulmonary function measurements were corrected to body temperature, pressure and water saturation.

One-second forced expiratory volume (FEV_1) and forced expiratory flow 25–75 (FEF_{25-75}) were obtained by standard techniques (16). The working FEV_1 was obtained as the mean from the best three of five tracings as recommended by the Division of Lung Diseases, NHLBI (15). FEF_{25-75}'s were obtained from the same tracings, and a mean was calculated. The working means were converted into per cent predicted values using the nomograms of Dickman et al. (17) for subjects less than age 25 years and those of Ferris et al. (18) for subjects 25 years and older.

In addition to the retrospective respiratory symptom and illness histories obtained at each subject's entrance into the study, the acute respiratory illness experience for the five through nine-year-old children was assessed prospectively over a two-year period using methods previously described (19). Briefly, parents of children were called by telephone every two weeks (except in July and August) for the two-year period September, 1975, through June, 1977. Those children who had experienced one or more selected respiratory symptoms in the previous two weeks were visited in their homes for a more detailed history of their respiratory symptoms. Definitions of upper and lower respiratory illness were identical to those proposed by Monto (20).

Definitions of cigarette smoking

Adults (age 20 years and older). Adults were defined as having never smoked if they never smoked or smoked less than one cigarette per day for more than one year, or less than 20 packs during their lifetime. Current smokers were defined as those who smoked more than these amounts and who were smoking within one month of the time of interview. Ex-smokers were persons who had stopped smoking more than one month before the time of interview and who had smoked more than the above amounts.

Children (age 19 years or younger). Children were considered to have never smoked if they never smoked as much as one cigarette per week. They were classified as ever-smokers if they were currently smoking or had at some time smoked as much as one cigarette per week.

Analysis of data

Households were divided into three groups on the basis of parental smoking

pattern (table 2). and only those for which interview data were available for both parents have been included in this analysis. Households in which only one parent was interviewed were excluded since, for the purposes of this analysis, it was necessary to have accurate smoking histories for both parents throughout the lifetime of the children in the household. FEF_{25-75} was used in the present analysis because it provided better dis-

crimination between children in the various household smoking groups than did FEV_1. Initial age-sex standardization was carried out using the nomograms referred to previously. However, it was observed that the variability around the mean FEF_{25-75} per cent predicted ($FEF_{25-75}\%$) was high (1 SD > 20%). Therefore, to decrease the variability of the $FEF_{25-75}\%$ measurement, and thereby increase the efficiency of the analysis and provide a more direct means of comparing children in different age-sex categories, an $FEF_{25-75}\%$ score (FEF-Z score) was derived as follows: Children were divided into sex-specific, five-year age groups, and adults divided into two sex-specific groups. Within each group, subjects were rank ordered and the ranks converted into a cumulative frequency distribution. Each rank was then assigned a score from a table of areas under a standard normal curve (21). Each score corresponded to the position of the rank in the cumulative frequency distribution. The mean score within each group was thus 0 with a variance of 1. The scores can, for example, be interpreted as follows (figure 1): persons with a score of +1 would have an $FEF_{25-75}\%$ equal to or greater than 84 per cent of the members of their age-sex spe-

TABLE 2

Classification of households on the basis of parental smoking pattern. East Boston, MA, 1974

Two "never" smoking parents (type 0)
 a. Both parents never smoked.
or
 b. One or both parents ex-smokers but neither smoked at any time during the lifetime of all children.

Two "current" smoking parents (type 2)
 a. Both parents current smokers and smoked during first year of life of all children*
or
 b. One or both parents ex-smokers but both smoked during first year of life of all children.

One "current" smoking parent (type 1)
 a. One "never" and one "current" parent smoker, as defined above.

* No current smokers excluded on this basis.
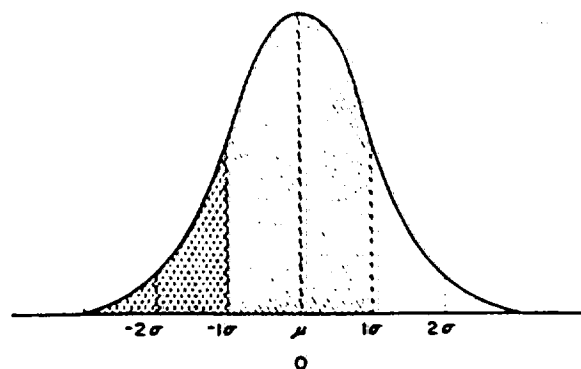
FIGURE 1. Interpretation of FEF-Z score. The FEF-Z scores are normally distributed with a mean (μ) of 0 and variance (σ^2) of 1. Subjects with a score of 1 (1σ) would have an $FEF_{25-75}\%$ predicted equal to or greater than 84 per cent of their peers (hatched + cross-hatched areas). Subjects with a score of -1 (1σ) would have an $FEF_{25-75}\%$ equal to or greater than only 16 per cent of their peers (cross-hatched area).

cific group; persons with a score of -1 would have an $FEF_{25-75}\%$ equal to or greater than only 16 per cent of their group. Linear regression (22, pp. 135-147) of FEF-Z score on age failed to show any trend toward age ordering of the ranks within each age-sex specific group for subjects aged 5-19 years (all except three children were age 19 years or younger).

A weighted mean FEF-Z was obtained for the children of each household included in the analysis. The weights were derived from a one-way analysis of variance (22, pp. 279-285) which had demonstrated familial similarity of level of FEF-Z score. The effect of the weighting procedure is to take into account the varying size of sibships in the calculation of the overall means (see Appendix).

All tests of statistical significance have been reported as one-sided p values. The use of one-sided p values was felt to be justified since the alternative hypothesis of a protective effect of parental smoking on pulmonary function of children did not seem plausible.

Selection of households for analysis

The 444 index children initially entered into the study (table 1) came from 404 households. In 318 of these households (79.0 per cent), both parents were living in the household at the time of survey. Two-

hundred and forty-six of these 318 households (77.4 per cent) had complete data collected for both parents (in 70 households, the fathers refused to be interviewed, and in two, the mothers refused). These households where only one parent was interviewed were comparable to those where both parents were interviewed in terms of number of children per household interviewed (2.5 vs. 2.5), children's age in years (median, 8.4 vs. 8.4), and sex of children (per cent male, 52 vs. 53), per cent of children who had never smoked (19.6 per cent vs. 17.3 per cent), density of people in the household (persons per room, 0.84 vs. 1.00), type of heating system in the house (per cent gas, 33.8 vs. 29.3), and the level of education of the interviewed parents (per cent with high school diploma, 43.1 vs. 45.9).

Of the 246 households with data for both parents, 154 (62.6 per cent) had adequate smoking history and pulmonary function data for at least one child in the household. Ninety-two households where both parents were interviewed were excluded because no child in the household had data for both pulmonary function and smoking history. In table 3, the characteristics of the 92 excluded households are compared with those of the 154 included in the study. Children from excluded households were younger and came from households where fewer chil-

TABLE 3

Characteristics of East Boston, MA, households for which both parents were interviewed, January-June, 1975

Comparability factor	Included in present analysis	Excluded from present analysis
No. of households	154	92
Children/household interviewed	3.06	1.45
% male children	57.4	56.3
Median age in years of children (range)	9.4 - 25†	6.4 - 15†
Median persons/room (range)	1.0(0.5 - 2.0)	0.8(0.3 - 2.0)
% with gas heater	32.9	26.4
% of parents with high school diploma	35.6	45.4†

* Only three subjects older than age 19 years.

† Difference not significant.

dren per household had been interviewed. In other respects, these households were comparable to those included in the analysis.

A further 29 per cent of the 445 children of all ages available from the 154 households which form the basis of this report had missing data for pulmonary function and/or smoking history and, therefore, could not be included in the present analysis. Children who were excluded for these reasons were younger (median age, 8 years; mean age, 8.4 ± 3.6 years) than children available for analysis (median age, 10 years, mean age, 10.3 ± 3.7 years) but were comparable with regard to sex distribution (per cent male, 54.4 vs. 52.2). There were 87 children who were excluded only because of missing pulmonary function data. Thirty-seven of these children from types 0 and 1 households (table 2) had smoking histories which were comparable to children included in the analysis (never, 81.1 per cent vs. 82.1 per cent; ever, 18.9 per cent vs. 17.9 per cent) and their median age (9 years) closely approximated that of children in the analysis. Fifty excluded children were from type 2 households and had a lower rate of personal cigarette smoking than those included in the analysis (ever, 12.0 per cent vs. 21.9 per cent). This is ac-

counted for by the fact that 34 (68.0 per cent) of these 50 children were aged nine years or less and had never smoked (median age for all 50 children, 7.5 years). This rate of smoking compares with a rate of having ever-smoked of 6.6 per cent in the children aged nine years or less included in the analysis ($p = 0.124$, Fisher's Exact Test).

RESULTS

Children from type 0 households (table 2) who themselves had never smoked cigarettes had higher average levels of FEF-Z scores than children from type 1 or type 2 households who never smoked (table 4, "all sibships"). Average FEF-Z scores differed by 0.156 and 0.355 standard deviation units between type 0 households and type 1 and 2 households, respectively. Although none of the specific differences are statistically significant (table 4), the trend is consistent with a decreasing level of function in the children with increasing parental smoking (χ^2 trend = 3.316; $p = 0.035$).

An identical result to that observed above is obtained if the analysis is restricted to children who never smoked and who also did not have any siblings who smoked (table 4, "sibships with only non-smoking children"). The comparable

TABLE 4

Level of FEF-Z score for children who had never smoked, East Boston, MA, 1975[*]

	All sibships, by household type			Sibships with only non-smoking children, by household type			Sibships with siblings who smoked, by household type[‡]	
	0	1	2	0	1	2	1	2
Average FEF-Z score	0.357†	0.201‡	0.002	0.357	0.194§	0.046	0.222	-0.173
No. children	26	75	160	26	57	115	16	45
No. households	15	41	90	15	31	66	10	24

* Eight households contained only children who had ever smoked, and they are not included in this table.
[‡] No children in type 0 households ever smoked and, therefore, type 0 households are not included under this heading.
† $t_{(x)}$ = 1.530, p = 0.05 for difference 0.357 - 0.002. $t_{(x)}$ = 1.314, p = 0.20 for difference 0.357 - 0.046
‡ $t_{(x)}$ = 0.627, p = 0.25 for difference 0.357 - 0.201.
§ $t_{(x)}$ = 0.630, p = 0.25 for difference 0.357 - 0.194

differences between the households are 0.163 and 0.311, respectively. Again, the specific differences are not statistically significant but a clearly consistent trend is observed (χ_1^2 trend = 2.002; p = 0.079). This second analysis was carried out since some children who reported that they had never smoked might have smoked and this would most likely occur in families where there were also children who had ever smoked (2). Such misclassification would serve to exaggerate differences between the different parent-smoking household categories. That this may have occurred to some extent is suggested by the observation that the average level of FEF-Z score was lower for children who never smoked and who lived with smoking siblings at least in type 2 households (table 4, "sibships with siblings who smoked").

Compared to children who had never smoked, children who had ever smoked had lower levels of pulmonary function regardless of whether one or both parents were current smokers (table 5). In type 2 households, the FEF-Z score for smoking children was 0.355 standard deviation units lower than that for non-smoking children (-0.309 vs. 0.046, t_{51} = 1.797, p = 0.035). A similar comparison for type 1 households gave a difference of 0.429 standard deviation units (-0.235 vs. 0.194, t_{31} = 1.533, p = 0.065). When smoking children were compared to non-smoking children who came from type 0 households, mean FEF-Z scores differed by 0.666 (-0.309 vs. 0.357, t_{50} = 2.432, p = 0.01) and 0.592 (-0.235 vs. 0.357, t_{24} = 1.863, p = 0.035) standard deviation units for type 2 and type 1 households, respectively.

The possibility that the lower levels of FEF-Z scores in children of smoking parents were the result of an increased burden of respiratory illness was investigated. At entrance into the study, parents of children aged 5–9 years were asked if their child had ever had a doctor's diagnosis of acute bronchitis, pneumonia, croup or bronchiolitis, and the age at which each was first diagnosed (table 6). There was no consistent tendency for the respiratory illness burden to increase with increasing parental cigarette smoking, although the number of type 0 households is too small for a definitive statement.

TABLE 5

Level of FEF-Z score for children who had ever smoked by household type, East Boston, MA, 1975

	Household type[*]	
	1	2
Average FEF-Z score	-0.235	-0.309
No. children	20	37
No. households	13	27

[*] There were no children who ever smoked in type 0 households

TABLE 6

Respiratory illness[*] reported to have occurred prior to entrance into the study for East Boston, MA, children aged 5–9 years[+], as reported at interview of parents, January–June, 1975

	Household type		
	0	1	2
1st illness before age 1 year	1 (8.3)	8 (21.6)	7 (8.5)
No. households	12	37	82

[*] Acute bronchitis, pneumonia, croup and bronchiolitis reported in response to the question: "Has a doctor ever told you that ___ had ___?"

All children aged 5–9 years in the various household groups for whom such data were available are included, regardless of whether or not they were included in the analysis of pulmonary function.

[+] Per cent

Further confirmation of a lack of association of parents' smoking and respiratory illness frequency is found in table 7. The cumulative two-year respiratory illness frequency as determined directly in a prospective study was very similar for children in the three parent smoking categories. Moreover, there was no trend toward increasing illness burden with an increasing number of parents who smoked.

Indices of household crowding and type of home heating system were also measured. The mean number of persons per room was virtually identical for the three household types (type 0 = 1.04, type 1 = 1.10, type 2 = 1.00). Analysis of the number of homes with central gas heating systems in kitchens (a common type of home heating system in East Boston) showed that type 2 households had a smaller percentage of such systems (23.7 per cent) than type 0 (54.5 per cent) and type 1 households (78.3 per cent).

Attempts to directly monitor the indoor environments of the three parent smoking groups for levels of various air pollutants were unsuccessful because we were unable to obtain the cooperation of a sufficient number of households. Data from previous work in East Boston (13) have shown that there are no overall differences in outdoor air quality in various parts of the community.

DISCUSSION

The data presented in this report indicate that the cigarette smoking habits of parents may have a measurable effect on the pulmonary function of their non-smoking and smoking children. The effect is predominantly due to parental smoking and is not due to the confounding effect of the children's smoking habits. The average level of age-, height- and sex-standardized FEF_{25-75} of children who had never smoked declined progressively between families with two parents who had never smoked through families with two currently smoking parents (table 4). The average decline in FEF_{25-75} ranged between 0.15-0.20 standard deviation units with the addition of each smoking parent to the household. Moreover, the difference in the average level of FEF_{25-75} was as large between non-smoking children with two non-smoking parents (type 0 households) and similar children with two smoking parents and no smoking siblings (0.311 standard deviation units) as it was between smoking and non-smoking children with two smoking parents (type 2 households, 0.355 standard deviation units).

Although some of the specific comparisons between the parent-smoking household groups did not achieve statistical significance, the patterns of decline in

TABLE 7

Total two-year respiratory illness experience for children aged 5 - 9 years, by parent smoking category, East Boston, MA, 1975-1977*

No. of illness(es)	Parent smoking category		
	Type 0	Type 1	Type 2
0-1	2(8.7)†	17(21.3)	20(21.3)
2-3	7(30.4)	31(38.8)	31(33.0)
>3	14(60.9)	32(40.0)	43(45.7)
Total	23	80	94

* Includes upper and lower respiratory illnesses and episodes of isolated cough (20). All children aged 5-9 years in the various household groups for whom such data were available are included, regardless of whether or not they were included in the analysis of pulmonary function.
† Per cent of column total—males and females combined because their rates were not significantly different ($\chi^2 = 3.920; p = 0.417$).

levels of the standardized FEF_{25-75} were consistent in all the analyses. Those comparisons which reflected the extremes of what might be considered a dose-response relationship between parental smoking and the children's level of FEF_{25-75} (e.g., nonsmoking children of two non-smoking parents vs. smoking children of two currently smoking parents) did achieve statistical significance.

The question of the validity of the observations reported bears directly on the nature of the sample of subjects used in the present analysis and the method for standardizing FEF_{25-75}. Families excluded because only one parent was interviewed were comparable to families with two parents interviewed with regard to important demographic and smoking variables. A potential problem does exist in the 154 two-parent families finally selected for analysis. Children from these families who were excluded due to missing pulmonary function and/or smoking history data were younger and, consequently, smoked less than those used in the analysis. Most of these differences were accounted for by the children excluded in the type 2 families. These excluded children could have biased the results only if their relative youth and lack of smoking experience diminished or enhanced their susceptibility to the effects of their parents' smoking. There is no evidence to suggest the former possibility, nor does it seem likely. Any enhanced susceptibility which these excluded type 2 children might show would tend to increase the strength of the reported associations. Therefore, our results could be biased toward an underestimate of the true magnitude of the observed relationship.

The use of the FEF-Z score is not likely to account for the observed results. Preliminary analysis demonstrated that there was no age ordering of the scores either within each age group or in the entire group aged 5 – 19 years (i.e., the group

that included all but three of the children in this analysis). Thus, any minor age differences between the three household groups could not account for the findings in this study. Although the use of the FEF-Z score does not permit a direct conversion back to a flow rate, this is not a serious limitation for the present report. The major interest here is in relative differences between groups of children. For this purpose, the score is ideal since it allows estimates of relative differences across a wide range of ages in terms of standard deviation units which are easily understandable.

Our findings differ from those of Schilling et al. (12), who addressed this problem but were unable to demonstrate any effect of parental smoking on the pulmonary function of children. Several factors might explain this variation. The definitions of parental smoking differed, with Schilling et al. (12) using only parents' current smoking as the criterion. Different measures of pulmonary function are also reported, and the disparity in the two sets of findings may reflect differences in the inherent ability of various measures of pulmonary function to distinguish between the groups of children. Finally, the analysis of variance used by Schilling et al. does not appear to properly correct for the differences in sibship size and the fact that there is a significant intraclass correlation of pulmonary function among siblings. These factors have been controlled in the present analysis.

The mechanisms that underlie the progressive decline in FEF_{25-75} with increasing parental smoking are conjectural. Our data do not suggest that an increased respiratory illness burden is the explanation, as has been suggested by others (7, 8, 10). Studies which have examined children in the first few years of life have consistently found an association between parental cigarette smoking and increased episodes of respiratory illness (7, 8, 10). The present data are retrospective in this

regard (table 6), and the number of type 0 households available for analysis was very small. Therefore, our data may not be as sensitive as those in studies which directly observed infants and very young children. Studies using populations of children comparable in age to our own have focused largely on the relationship of chronic symptoms (5, 9, 11) to smoking habits of adults, and their data are not comparable to ours. In one of these studies (5), which evaluated acute respiratory tract illness, data were collected retrospectively with no confirmation by prospective follow-up. A series of studies (4, 6), which focused on acute respiratory illness in relation to parental smoking, did show an association between an increased number of such illnesses in the children of smoking parents in the seven days preceding interview. It is difficult to compare such findings with our own, since the methods and period of observation are so different.

Although the assessment of socio-economic status and individual household environment is incomplete, our limited data do not suggest that differences in these variables play a major role in explaining the results we obtained. Indices of crowding were comparable in the three household groups. Type 2 households were least likely to have large gas-burning heating units in their homes. Finally, the range of socioeconomic status, as indicated by job and level of education, is limited in the study community. Because of the small number of type 0 households, a meaningful analysis of these factors could not be undertaken.

The possibility that contamination of indoor air by cigarette smoke may play a part in our findings has not been systematically explored. We were unable to determine satisfactorily to what extent the atmospheres of the homes of the various household groups differed. However, others (3, 23, 24) have demonstrated that cigarette smoke contaminates indoor air to a substantial extent and that substantial amounts of respirable particulates such as tar and nicotine, as well as carbon monoxide and other gases can be detected. The mechanisms by which this contamination might affect the lungs of nonsmokers have not been well studied. Tars have been shown to be allergens capable of inducing precipitin reactions in rabbits (25), and, although it is not believed to be an allergen itself, nicotine may be able to function as a hapten when combined with other substances (26). Becker et al. (27, 28) have isolated a glycoprotein present in tobacco smoke to which human volunteers demonstrate cutaneous hypersensitivity and which is capable of activating Factor XII (Hageman factor). They postulate that the glycoprotein may trigger an inflammatory response via activation of Factor XII which might be related to the pulmonary injury associated with cigarette use. Furthermore, the amount of this antigen in smoke is such that it may be capable of exerting its effects in adjacent non-smokers as well. Surely, a great deal more work will be needed to clearly define the risks to the lungs of nonsmokers.

At present, obviously, it is impossible to know the long-range health effects of the observations reported here regarding the passive effects of parental smoking. The long-range effects are the focus of the prospective portion of this study as it continues over time.

In addition, although this report has focused on the passive effects of parental smoking, it is important to remember the very direct effect of the children's own smoking habits on their relative levels of FEF_{25-75}. These data lend additional support to observations made in teenagers (29, 30) that cigarette smoking in children has measurable functional consequences despite limited daily and total cigarette consumption. Additional data

are being collected in the East Boston population to explore this problem in more depth.

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APPENDIX

A. One-Way Analysis of Variance-Random Effects Model

1. $Y_{ij} = \mu + A_i + e_{ij}; A_i \sim N(0, \sigma_1^2), e_{ij} \sim N(0, \sigma^2)$,

where Y_{ij} = FEF-Z score for the jth person in the ith household,

μ = mean FEF-Z score for the population,

A_i = random effect due to family, and

e_{ij} = random effect for jth person in ith family.

2. $Y_i = \mu + A_i + \bar{e}_i$

where Y_i = the average FEF-Z score for the ith family,

A_i = as above, and

$\bar{e}_i$ = random effect within the ith family and = $\Sigma e_{ij}/N_i$

and variance $(Y_i) = \sigma_1^2 + \sigma^2/N_i$

where N_i = number of persons in ith family.

3. $\bar{\bar{Y}} = \Sigma w_i Y_i / \Sigma w_i$

where $w_i = 1/(\sigma_1^2 + \sigma^2/N_i)$

and variance $(\bar{\bar{Y}}) = 1/\Sigma w_i$

B. Example of Weighting Procedure

From 1 Way ANOVA $\sigma^2 = 0.723$ $\sigma_1^2 = 0.230$

Family	No. in ith Family	$\bar{Y}_i$	w_i	$w_i Y_i$
1	1	1.889	1.049	1.982
2	2	-0.191	1.691	-0.323
3	3	1.255	2.123	2.664
			$\Sigma w_i = 4.863$	$\Sigma w_i Y_i = 4.323$

$\bar{\bar{Y}} = \dfrac{4.323}{4.863} = 0.889$

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Weiss, S.T., Tager, I.B., Speizer, F.E., Rosner, B. "Persistent Wheeze: Its Relation to Respiratory Illness, Cigarette Smoking, and Level of Pulmonary Function in a Population Sample of Children" American Review of Respiratory Disease 122: 697-707, 1980.

SUMMARY: In a study of early-life risk factors for the development of adult obstructive airway disease, respiratory symptoms, disease and smoking histories, and spirometry were obtained for 650 children 5 to 9 yr of age and their families in East Boston, Massachusetts. Persistent wheezing was the most frequently reported chronic symptom, occurring in 9.2% (60/650) of the population. Children with persistent wheezing were more likely to report cough and phlegm (p<0.001), a history of asthma (p<0.001), hay fever (p<0.02), or past hospitalization with a respiratory illness (p<0.001) than their asymptomatic peers. Prospective evaluation of a subsample of the 650 children confirmed a greater occurrence of acute lower respiratory illness in those children with persistent wheeze. Parental cigarette smoking was linearly related to the occurrence of persistent wheeze (p=0.012) and lower degrees of mean normalized forced expiratory flow during the middle half of the forced vital capacity (FEF-Z score). A multiple linear regression identified the mother's current smoking status and current persistent wheeze as significant predictors of the children's mean FEF-Z score. Other variables, such as the father's smoking, children's personal smoking, a doctor's diagnosis of asthma, and a past history of lower respiratory illness were not significant predictors of the FEF-Z score.

Persistent Wheeze

Its Relation to Respiratory Illness, Cigarette Smoking, and Level of Pulmonary Function in a Population Sample of Children[1-3]

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SUMMARY

In a study of early-life risk factors for the development of adult obstructive airway disease, respiratory symptoms, disease and smoking histories, and spirometry were obtained for 650 children 5 to 9 yr of age and their families in East Boston, Massachusetts. Persistent wheezing was the most frequently reported chronic symptom, occurring in 9.2% (60/650) of the population. Children with persistent wheezing were more likely to report cough and phlegm ($p < 0.001$), a history of asthma ($p < 0.001$), hay fever ($p < 0.02$), or past hospitalization with a respiratory illness ($p < 0.001$) than their asymptomatic peers. Prospective evaluation of a subsample of the 650 children confirmed a greater occurrence of acute lower respiratory illness in those children with persistent wheeze. Parental cigarette smoking was linearly related to the occurrence of persistent wheeze ($p = 0.012$) and to lower degrees of mean normalized forced expiratory flow during the middle half of the forced vital capacity (FEF-Z score). A multiple linear regression identified the mother's current smoking status and current persistent wheeze as significant predictors of the children's mean FEF-Z score. Other variables, such as the father's smoking, children's personal smoking, a doctor's diagnosis of asthma, and a past history of lower respiratory illness were not significant predictors of the FEF-Z score.

Introduction

The most important risk factor for the development of chronic respiratory symptoms and airflow obstruction in adults is cigarette smoking (1). However, a small number of adults with chronic airflow obstruction have never smoked, and many lifelong smokers never develop respiratory symptoms or clinical evidence of chronic airflow obstruction. The explanation for this individual susceptibility to the effect of direct exposure to cigarettes is unknown (2). Among the factors studied to date in adult populations, e.g., σ-antitrypsin polymorphism (3), atopic diathesis (4), and a retrospective history of childhood respiratory illness (5, 6), none has provided clear insights into this susceptibility.

Epidemiologic studies of respiratory disease in children have demonstrated that children with chronic respiratory symptoms have lower degrees of pulmonary function (7, 8). The hypothesis that factors such as lower respiratory illness, atopic

diathesis, and cigarette smoking acting during childhood may be important in the subsequent development of chronic airflow obstruction in adult life has been suggested. As part of a prospective study of early-life risk factors for the development of chronic airflow obstruction, we determined the relation of chronic respiratory symptoms (current persistent wheeze and chronic cough and phlegm) to the occurrence of lower respiratory illness, atopic diathesis, personal and parental cigarette smoking habits, and the level of pulmonary function in a population sample of children.

Methods

Selection of sample. A random sample was taken of all children 5 to 9 yr of age (index children) in the public and parochial schools of East Boston as of September 1974 (Twenty-two children 4 yr of age and 5 children 10 yr of age were included in the sample because they appeared on the school registration lists from which the sample was actually drawn). Thirty-two per cent of all children in each school in the study community were randomly chosen to ensure a uniform geographic distribution in the study population. The number of children initially selected for study was based on estimates of expected refusal rates and on the estimated sample needed for a follow-up of familial patterns of chronic productive cough as determined from a previous study in this community (9).

East Boston is a geographically defined neighborhood within the city of Boston. Its inhabitants are of predominantly Italian-American descent. Sixty-three per cent of the working adults in the study sample were clerks (or in related positions), craftsmen, service workers, or one of the other operatives defined by the U.S. Census (10). Five per cent of them held professional, technical, or managerial positions. Approximately 40% of the adults had a high school diploma.

Screening of sample. The households of the selected children were visited between January and June 1975 by specially trained interviewers (trained using materials provided by the Division of Lung Diseases, National Heart, Lung and Blood Institute), and the persons in the households were enumerated. All members of the household were then asked to attend a special neighborhood clinic for the purpose of obtaining respiratory symptom and illness histories and measures of pulmonary function. Those families who agreed to participate but did not come to the clinic were interviewed at home. Standardized questionnaires were used to obtain histories and demographic data for all members of the household. Separate questionnaires were administered by the interviewers for subjects younger than 10 yr of age and for those older than 10. Questions relating to chronic cough, phlegm, and chest illness were those proposed by the Division of Lung Diseases, National Heart, Lung and Blood Institute (11). Mothers answered all questions for children 10 yr of age or younger except those

questions pertaining to the child's smoking history. Smoking histories were obtained from children individually in the absence of their parents during the pulmonary function testing.

In addition to the respiratory symptom and retrospective illness histories obtained for all index children and their siblings at entrance into the study, the acute respiratory illness experience for the index children was assessed prospectively over a 2-yr period using methods previously described (12). Briefly, parents of the index children were contacted by telephone every 2 wk (except in July and August) for the 2-yr period from September 1975 through June 1977. Index children who experienced one or more selected respiratory symptoms in the previous 2 wk were visited in their homes, and a more detailed history of their respiratory symptoms was obtained. Definitions of upper and lower respiratory illness were identical to those proposed by Monto and associates (13), with the exception that the lower respiratory episodes characterized by wheeze as the sole criteria were not counted as lower respiratory illness.

Definitions of respiratory symptoms and illnesses. Current wheezing was assessed on the basis of the following questions posed by the interviewers:

"Does _____'s breathing ever sound wheezy or whistling?"

(1) No. If yes, ask: (2) Does this occur only with colds? (3) Does this occur occasionally apart from colds? (4) Does this occur most days or nights? (5) Does this occur with colds and occasionally apart from colds?

For the purpose of this report, the absence of current wheezing was defined as a response of "no" or wheezing "only with colds." Children with wheezing "occasionally apart from colds" only were excluded from the analysis. Current persistent wheezing was defined as wheezing that occurred "with colds and occasionally apart from colds" or "most days and nights."

Chronic cough and phlegm was defined as cough and sputum production for any 3 months in any 1 year.

Specific respiratory illnesses were defined in terms of parental response to each of the following questions:

"Has a doctor ever told you that your child has ever had. . . . (1) asthma? (2) hay fever? (3) eczema? (4) croup? (5) bronchitis? (6) bronchiolitis? (7) pneumonia?"

The age at the time of first diagnosis and the total number of episodes of each illness were also recorded.

The presence of an atopic diathesis was defined as a positive response to the questions: "Has a doctor ever told you that you had . . . (a) hay fever? (b) asthma? (c) eczema?" (Each asked separately.)

Definitions of cigarette smoking. A parent was defined as having never smoked if she/he never smoked, smoked less than 1 cigarette per day, or smoked less than a total of 20 packs during her/his lifetime. A current smoker was defined as one who smoked more than the above amount and was smoking within 1 month of the time of interview. Ex-smokers were defined as persons who had stopped smoking more than 1 month before the time of

the interview, and had smoked more than the above amounts previously.

Households were classified as nonsmoking if both parents were "never" smokers. Smoking households were divided into those in which both parents were "current" smokers and households in which only 1 parent was a "current" smoker and the other parent either a "never" smoker or an ex-smoker. Households in which only a single parent was interviewed were excluded from this analysis.

A child was considered to have never smoked if he or she never smoked. A child was classified as an ever-smoker if he or she had at sometime smoked a cigarette, regardless of amount, as determined by response to a series of standardized questions asked in the absence of parents.

Pulmonary function testing. Forced vital capacity (FVC) maneuvers were performed in the sitting position without a noseclip, using an 8-L, water-filled, portable recording spirometer (Survey Spirometer; Warren Collins, Inc., Braintree, MA). A tracing was considered acceptable if it was at least 4 s in duration and if the interviewer felt that a maximal effort had been made. All tests on children were done by 1 or 2 interviewers, each with at least 2 yr of experience. Standing height was measured without shoes to the nearest one half inch. Forced expiratory volume in one second (FEV_1) and forced expiratory flow during the middle half of the FVC (FEF_{25-75}) were obtained by standard techniques (14). After correcting volumes to BTPS, per cent predicted values were obtained using the nomograms of Dickman and co-workers (15).

Analysis of data. The $FEF_{25-75\%}$ was used in the present analysis because it provided better discrimination between children in the various household smoking groups than did the FEV_1. Initial age-sex standardization was carried out using the nomograms referred to previously. However, it was observed that the variability about the mean FEF_{25-75} per cent predicted ($FEF_{25-75\%}$) was high (1 SD > 20%). Therefore, to decrease the variability of the $FEF_{25-75\%}$ and to increase the efficiency of the analysis, a score (FEF-Z score) was derived as follows: Children were divided into sex-specific, 5-yr age groups. Within each group, subjects were rank ordered, and the ranks were converted into a cumulative frequency distribution. Each rank was then assigned a score from a table of areas under a standard normal curve (16). The mean score within each group was thus 0 with a variance of 1. The scores can be interpreted as follows (figure 1): persons with a score of +1 had a $FEF_{25-75\%}$ equal to or greater than 84% of the members of their age- and sex-specific group; persons with a score of −1 had a $FEF_{25-75\%}$ equal to or greater than only 16% of their group. Linear regression (17) of the FEF-Z score on age failed to show any trend toward age-ordering of the ranks within each age- and sex-specific group for subjects 5 to 19 yr of age (all except 3 children were 19 yr of age or younger). Only children 5 to 9 yr of age were included in subsequent analyses.

A weighted mean FEF-Z score was obtained for the children in each household included in the analysis. The weights were derived from a random effects analysis of variance model (18), which had demonstrated a significant familial clustering of the FEF-Z score. The effect of the weighting procedure is to take into account the varying size of sibships in the calculation of the overall means (19).

When appropriate, comparisons were performed with the chi square test with a correction for continuity unless estimated cell size was less than 5, in which case Fisher's exact test was used. A step-down multiple linear regression model was used to assess the effect of a number of variables on the children's FEF-Z score (20).

Inclusion of subjects in analyses. The outcome of the overall sample selection used for this study has been presented in detail elsewhere (19).

Although respiratory symptom and illness questionnaires were completed for 650 children 5 to 9 yr of age, not all of these children had data available for smoking history and pulmonary function. Furthermore, because of the combination of subject refusal and the existence of single parent households, smoking data were not available for both parents in all households. To identify possible bias due to excluding subjects in the analyses, the comparability of various subject groups was assessed.

Personal smoking history data were available for only 67% of the study children. The percentage of nonrespondents to the questions about personal smoking was not significantly different for children with current persistent wheeze (28.3%, 17/60) from those without this symptom (33.9%, 193/569).

Smoking history data for both parents in the household were available for 51.7% (31/60) of children with current persistent wheeze, and 59.9% (341/569) of children without this symptom (p = NS). The availability of these data also was not significantly different for children with and without the symptoms of chronic cough and phlegm (52.4%, 11/21 versus 61.2%, 372/608).
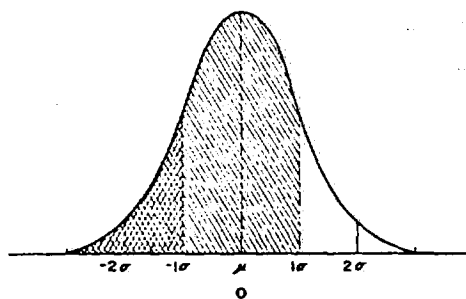
Fig. 1. Interpretation of the FEF-Z score. The FEF-Z scores are normally distributed with a mean (μ) of 0 and a variance (σ^2) of 1. Subjects with a score of 1 (1σ) would have an $FEF_{25-75\%}$ equal to or greater than 84% of their peers (*hatched and cross-hatched areas*). Subjects with a score of −1 (−1σ) would have an $FEF_{25-75\%}$ equal to or greater than only 16% of their peers (*cross-hatched area*) (19).

TABLE 1

AGE-SEX DISTRIBUTION OF THE INDEX CHILDREN AND THEIR SIBLINGS
SURVEYED FOR RESPIRATORY ILLNESS SYMPTOMS IN EAST BOSTON, MASS.,
JANUARY–JUNE 1975

| | Index Children | | Siblings | | Total In Each Age Group |
Age	Male	Female	Male	Female*	
4	11	10	0	1	22
5	35	38	17	25	115
6	56	38	12	14	120
7	54	35	19	23	131
8	51	46	24	20	141
9	38	24	21	27	110
10	5	3	1	2	11
	250	194	94	112	650

* χ^2 for difference between males and females = 3.94; p = NS.

Forced expiratory volumes were performed satisfactorily by 60.8% (395/650) of the study children. Children with and without pulmonary function data were comparable with regard to sex distribution, average number of siblings per household, parent smoking history, type of home heating system, reporting of a doctor's diagnosis of asthma, and the reporting of current persistent wheeze. Children with missing data were significantly younger than those for whom function data were available, and they were significantly less likely to have ever smoked cigarettes.

Results

Six-hundred fifty children, 4 to 10 yr of age, from 414 families were interviewed. There were 444 index children and 206 of their siblings (table 1). The age distribution for the male and female chil-

TABLE 2

A HISTORY OF PAST OCCURRENCE OF RESPIRATORY ILLNESS AND
SYMPTOMS IN CHILDREN 5 TO 9 YR OF AGE BASED ON
QUESTIONNAIRES ADMINISTERED AT THE INITIAL INTERVIEW

Illnesses and Symptoms	Males Number (%)	Females Number (%)	Total (%)
Acute respiratory illness			
Croup	48 (14.0)	33 (10.8)	81 (12.5)
Bronchiolitis	3 (0.9)	2 (0.7)	5 (0.8)
Acute bronchitis	69 (20.1)	58 (19.0)	127 (19.5)
Pneumonia	44 (12.8)	41 (13.4)	85 (13.1)
Atopic illness			
Hay fever	7 (2.0)	5 (1.6)	12 (1.8)
Asthma	26 (7.6)	13 (4.2)	39 (6.0)
Eczema	26 (7.6)	21 (6.9)	47 (7.2)
Chronic respiratory symptoms			
Cough and phlegm	8 (2.3)	13 (4.2)	21 (3.2)
Wheeze			
No wheezing or occasionally with colds	301 (87.5)	268 (87.6)	569 (87.5)
Wheezing occasionally apart from colds*	9 (2.6)	7 (2.3)	16 (2.5)
Wheezing with colds and occasionally apart from colds on most days and nights	32 (9.3)	28 (9.2)	60 (9.2)
Missing data*	2 (0.6)	3 (1.0)	5 (0.8)
	n = 344	n = 306	n = 650

* These children with intermediate wheeze status and missing data were excluded from all subsequent analyses.

dren was not significantly different (χ^2_4 = 3.94, NS). The mean age for male children was 7.0 yr, and the mean age for female children was 6.9 yr.

Acute respiratory illnesses were reported to have occurred with equal frequency in male and female children (table 2). Episodes of acute bronchitis were the most frequently reported acute respiratory illness (19.5%), followed by episodes of pneumonia (13.1%), a history of croup (12.5%), and a history of bronchiolitis (0.8%).

Atopic diseases (except asthma) were also reported with equal frequency in male and female children (table 2). Eczema was the most frequently reported atopic disease (7.2%), followed by asthma (6.0%) and hay fever (1.8%).

Asthma was reported more frequently for male children (7.6%) than for female children (4.2%), although this difference was not significant. Current persistent wheeze occurred equally in both sexes (9.3% versus 9.2%). The reported symptoms of chronic cough and phlegm production were also not significantly different for male and female children (2.3% versus 4.2%). The 5 children with missing wheeze data (including 3 children with a doctor's diagnosis of asthma) and the 16 children in the intermediate wheeze group (wheezing occasionally apart from colds) were excluded from all subsequent analyses.

Of the children for whom a doctor's diagnosis of asthma was reported, 63.9% (23/36) had persistent wheezing compared with 6.2% (37/593) of children for whom a doctor's diagnosis of asthma was not reported (χ^2_1 = 124.12, p < 0.001). Similarly, children with a history of asthma were significantly more likely to report the presence of chronic cough and phlegm (13.9%, 5/36) than children without a history of asthma (2.7%, 16/593) (p = 0.01, Fisher's exact test). Among

the nonasthmatic children with current persistent wheeze, 24.3% (9/37) reported the occurrence of chronic cough and phlegm compared with 1.3% (7/556) of the nonasthmatic children without persistent wheeze (p < 0.001, Fisher's exact test).

Children with current persistent wheeze had a significantly greater reported frequency of past episodes of acute bronchitis, pneumonia, and sinus trouble compared with children without current persistent wheeze (table 3). Moreover, children with persistent wheeze were significantly more likely to have been hospitalized in the past for a respiratory illness than children without current persistent wheeze (χ^2_1 = 31.52, p < 0.001).

Similarly, children with current persistent wheeze were more likely to report diseases considered to be atopic than children without this symptom (table 3). Asthma, hay fever, and eczema all were reported more frequently in the children with persistent wheeze.

Analysis of the prospective respiratory illness surveillance for the index children showed that 35% of all children experienced one or more lower respiratory illnesses in Year 1 and 22% of all children experienced such illnesses in Year 2 (table 4). Upper respiratory illnesses occurred in 36% of children in Year 1 and 21% of children in Year 2. Laryngotracheal illnesses were reported infrequently, 4% in Year 1 and 2% in Year 2.

For each year of the prospective surveillance, children for whom current persistent wheeze was reported at the initial interview experienced more lower respiratory illness than children without current persistent wheeze at the initial interview. The difference in the frequency of lower respiratory illness for children with and without current persistent wheeze was 15.6% for Year 1 and 21.9% for Year 2. In contrast, no significant dif-

TABLE 3

THE RELATION BETWEEN CURRENT PERSISTENT WHEEZE (PW) AND REPORTING OF RESPIRATORY ILLNESS AND ATOPIC DISEASE

	Children with PW (n = 60) (%)	Children without PW (n = 569) (%)	χ^2	p Value (%)
Acute bronchitis	19 (31.7)	102 (17.9)	5.74	0.017
Pneumonia	15 (25.0)	68 (11.9)	6.97	0.008
Sinus trouble	7 (11.7)	6 (1.1)	—	0.001*
Hospitalizations for respiratory illness	18† (30.0)	40 (7.0)	31.52	0.001
Asthma	23 (38.3)	13 (2.3)	—	0.001*
Hay Fever	4 (6.7)	6 (1.1)	—	0.02*
Eczema	5 (8.3)	40 (7.0)	—	NS*

* Fisher's exact test.
† For 13 of these 18 subjects, a doctor's diagnosis of asthma was reported.

TABLE 4

OCCURRENCE OF RESPIRATORY ILLNESS DURING A 2-YR PROSPECTIVE FOLLOW-UP OF THE INDEX CHILDREN—THE RELATIONSHIP TO CURRENT PERSISTENT WHEEZE

| | | Total Number of Children | Lower Respiratory Illness | | Upper Respiratory Illness | | Laryngotracheal Illness | |
				% of children with 1 or more episodes*		% of children with one or more episodes[†]		% of children with one or more episodes[‡]
Persistent Wheeze	yes	39		48.7		41.0		0.0
	no	350	Year 1	33.1	Year 1	35.7	Year 1	4.3
	Total	389		34.7		36.2		3.9
Persistent Wheeze	yes	38		42.1		21.1		2.6
	no	342	Year 2	20.2	Year 2	21.3	Year 2	2.0
	Total	380		22.4		21.3		2.1

* χ^2 for difference in number of lower respiratory illnesses for children with and without persistent wheeze: Year 1, $\chi_1^2 = 3.10$, $p < 0.10$; Year 2, $\chi^2 = 8.25$, $p = 0.004$.

[†] χ^2 for difference in number of upper respiratory illnesses for children with and without persistent wheeze: Year 1, $\chi^2 = 0.23$, NS; Year 2, $\chi^2 = 0.20$, NS.

[‡] χ^2 for difference in number of laryngotracheal respiratory illnesses for children with and without persistent wheeze: Year 1, Fisher's exact test, NS; Year 2, Fisher's exact test, NS.

ference was found for upper respiratory illness, when the difference in frequency was 6% for Year 1 and 0.2% for Year 2.

Demographic factors, which might have been responsible for the difference in occurrence of lower respiratory illness in subjects with current persistent wheeze, were investigated. There were no significant differences between children with and those without persistent wheeze for the following variables: percentage of homes with gas heaters in the kitchen (33% versus 31%), reported history of prematurity (7% versus 7%), and density of persons per room (the mean for families of children with persistent wheeze was 1.0 person/room versus 0.99 person/room for families of children without persistent wheeze.

The relation between the reporting of current persistent wheeze and the children's own smoking history is presented in table 5. Eight of 43 children with current persistent wheeze (18.6%) reported

that they had ever smoked cigarettes compared with 50 of 376 children (13.3%) who did not report this symptom (P = NS). In contrast, parental smoking habits were significantly related to the occurrence of current persistent wheeze (figure 2). Current persistent wheeze occurred in 1.85% (1/57) of children from households in which both parents never smoked cigarettes, in 6.85% (10/146) of children from households with 1 parent currently smoking, and in 11.8% (20/169) of children from households with 2 parents currently smoking (χ_1^2, trend = 6.36, p = 0.012). Chronic cough and phlegm were less closely related to parental smoking (figure 2), but followed a trend similar to that observed for current persistent wheeze. The percentages of children with chronic cough and phlegm were 1.7%, 2.7%, and 3.4%, respectively, for the 3 parent-smoking household groups (figure 2). When this analysis was repeated using those households in which

TABLE 5

THE RELATION BETWEEN CURRENT PERSISTENT WHEEZE* AND CHILDREN'S PERSONAL SMOKING HISTORY

| | Persistent Wheeze | | No Persistent Wheeze | | Total | |
	Number	(%)	Number	(%)	Number	(%)
Ever Smoked	8	(18.6)[†]	50	(13.3)	58	(13.8)
Never Smoked	35	(81.4)	326	(86.7)	361	(86.2)
Total	43	(100)	376	(100)	419	(100)

* 17/60 (28.3%) of children with current persistent wheeze and 193/569 (33.9%) of children without persistent wheeze did not answer the smoking questions.

[†] $\chi_1^2 = 0.521$ ($p > 0.30$) for the difference in the percentage of smoking children with and without current persistent wheeze.

RELATIONSHIP OF
CURRENT PARENTAL SMOKING STATUS
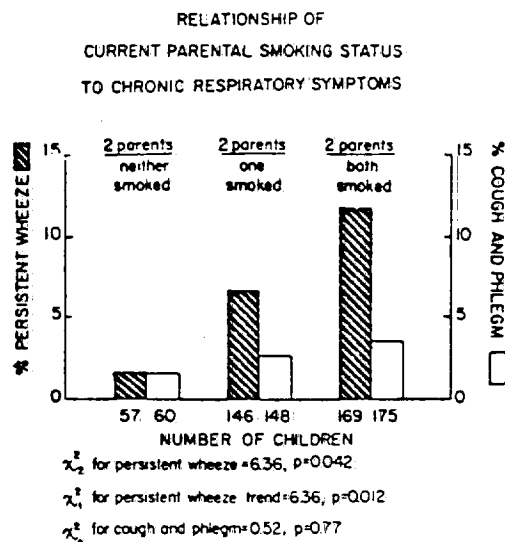TO CHRONIC RESPIRATORY SYMPTOMS

Fig. 2. Relation of current parental smoking status to chronic respiratory symptoms (persistent wheeze and cough and phlegm) in children. Both χ^2 values are the same since the total χ^2 was accounted for by the trend analysis.

mothers reported no symptoms of wheeze, the trend was the same. Children from households with 0, 1, or 2 smoking parents had prevalences of persistent wheeze of 0% (0/43), 1.8% (2/114), 7.7% (6/78), respectively (χ_1^2 trend = 6.109, p = .014). Analysis using households in which fathers did not wheeze gave prevalences of 0% (0/45), 6.7% (6/89), and 13.5% (10/74), respectively (χ_1^2 trend = 5.09, p = 0.025). Finally, analysis using households in which neither parent reported wheeze or chronic phlegm production gave prevalences of 0% (0/30), 3.6% (2/55), and 7.7% (2/26), respectively (χ_1^2 trend = 2.37, p > 0.2).

Children who reported current persistent wheeze had a significantly lower mean FEF-Z score than children without this symptom (−0.400 versus 0.060; table 6). After adjustment for the presence or absence of persistent wheeze, children with a present or past doctor's diagnosis of asthma had a lower mean FEF-Z score than children without such a diagnosis; however, the difference was not significant (table 6).

The relation of current persistent wheeze to the FEF-Z score also was examined by comparing the observed and expected prevalence of FEF-Z scores, which were 2 or more standard deviations below the population mean in children with and without this symptom. Three per cent (11/352) of the children without current persistent wheeze had scores 2 or more units below the mean, which is

not significantly different from the 2.3% predicted from the areas under a standard normal curve (16). In contrast, 14.0% (6/43) of those children with current persistent wheeze had scores 2 or more units below the mean (p < 0.01 by the 1-sample binomial test).

Of the 395 children who performed satisfactory FVC maneuvers, data for the smoking habits of both parents were available for 238 (60.3%). Children from households in which both parents had never smoked cigarettes had a mean FEF-Z score of 0.473, or a 0.522 standard deviation greater than the mean score of −0.049 observed in children from households in which both parents were current smokers (Z = 2.563, p = 0.005 for the one-sided test for significance of difference; table 7). Children from households in which only 1 parent was a current cigarette smoker had a mean FEF-Z score that was 0.075, or a 0.398 standard deviation lower than that observed for children with 2 nonsmoking parents (Z = 1.915, p = 0.028 for the 1-sided test for significance of difference). The difference between the mean score for children from households with 1 and 2 currently smoking parents was not significant (Z = 0.850, p = 0.198, one-sided test for significance of difference). Analysis for linear trend revealed that the progressive decline in the mean FEF-Z score with increasing parental smoking was significant (χ_1^2, trend = 5.709, p < 0.02).

Current smoking status of the mother (p = 0.017) and the presence of current persistent wheeze (p = 0.071) were the most significant predictors of a child's FEF-Z score (table 8). A doctor's diagnosis of asthma, the child's personal smoking history, and current smoking status of the father were not significant predictors of FEF-

TABLE 6

THE FEF-Z SCORES FOR CHILDREN WITH
OR WITHOUT CURRENT PERSISTENT WHEEZE BY
DOCTOR'S DIAGNOSIS OF ASTHMA

	Mean FEF-Z Score	Number
Persistent wheeze	−0.400*	43
Asthma†	−0.618	15
No asthma	−0.283	28
No persistent wheeze	+0.060	352
Asthma	−0.217	4
No asthma	+0.065	348

For mean FEF-Z score, see methods.
* Normal deviate for comparison of mean FEF-Z score for children with and without current persistent wheeze = 2.85, p = 0.004.
† Normal deviate for weighted average difference of mean FEF-Z score between asthma and no asthma in the persistent wheeze and no persistent wheeze groups = 1.306, p = 0.192.

TABLE 7

THE RELATION OF PARENTAL CIGARETTE SMOKING TO MEAN
FEF-Z SCORES IN CHILDREN 5 TO 9 YR OF AGE

	Two Parents Who Never Smoked	Two Parents, One of Whom is Current Smoker	Two Parents, Both of Whom are Current Smokers
Mean FEF-Z score	0.473*	0.075	−0.0491‡
Number of Children	33	94	111
Number of Siblings	26	67	78

* Normal deviate for the difference between mean FEF-Z score for the never smoking parent group and the 2 parent smoking group: $Z = 2.563$, $p = 0.005$, 1-sided test. Normal deviate for the difference between mean FEF-Z score for the never smoking parent group and the 1-parent smoking group: $Z = 1.915$, $p = 0.028$, 1-sided test.
† Normal deviate for the difference between mean FEF-Z score for 1-parent smoking and 2-parents smoking groups: $Z = 0.850$, $p = 0.198$.
‡ χ_1^2 for trend in mean FEF-Z score for parent smoking groups = 5.709, $p = 0.01$.

Z score. The total r^2 for the model was 0.08. An interaction variable (not shown in the table) for the mother's and father's current smoking also was not significant. Although lower respiratory illnesses were found to occur more frequently in children with persistent wheeze, this variable was not included in the regression model because of the relatively small number of persons with both persistent wheeze and such illnesses (table 4).

Discussion

The frequent reporting of current persistent wheeze observed in the present study was consistent with the finding of the Tuscon survey of a population of children and young teenagers (21). Our study also showed significant associations of persistent wheeze with a history of acute lower respiratory illness, history of atopic disease, and current parental cigarette smoking habit. Furthermore, this symptom was found to be associated with signi-

ficantly lowered degrees of pulmonary function, as measured by $FEF_{25-75\%}$.

The excess frequency of respiratory illness in subjects with persistent wheeze confirmed several British studies (8, 22, 23), which demonstrated that children with current chronic respiratory symptoms report a higher frequency of past lower respiratory illness than those children without chronic symptoms. The prospective respiratory illness surveillance conducted in the present study demonstrated that children with current persistent wheeze experienced a higher frequency of lower respiratory illness episodes than those children without persistent wheeze. This finding made it unlikely that the relation between current persistent wheeze and the past history of lower respiratory illness noted previously was due solely to selective recall on the part of the parents of the children with current persistent wheeze.

Although children with current persistent wheeze

TABLE 8

LINEAR REGRESSION MODEL FOR CHILDREN'S FEF-Z SCORE

Variable	Regression Coefficient*	Standard Error of Regression Coefficient	F Ratio	p Value
Intercept	+0.231	—		
Mother a current smoker	−0.308	0.128	5.77	0.017
Current persistent wheeze	−0.412	0.227	3.28	0.071
Doctor diagnosis of asthma in child	−0.420	0.266	2.51	0.114
Child's smoking history	+0.028	0.019	2.13	0.146
Father a current smoker	−0.046	0.145	0.10	0.750
			Total r^2 = 0.08	

* All independent variables defined as Yes = 1, No = 0; total subjects in the analysis = 238.

reported a history of atopic diseases more frequently than nonwheezing children, the degree to which this wheezing syndrome represented true atopy or alternative mechanisms of abnormal airway reactivity was unknown, and could not be determined from this study. Burrows and associates (24) found "wheezy bronchitis" to be associated with the occurrence of hyperreactivity to a battery of 5 skin test antigens. However, in general population surveys, a history of wheeze usually has been found to far exceed the reporting of a history of hay fever or asthma (21, 24). Moreover, recent investigations of airway reactivity to irritants whose effects are not thought to be related to an atopic mechanism (e.g., irritant gases at low concentration (25, 26), cold air (27), and viral illness (28-30)) suggested that alternative, nonatopic mechanisms indeed may be involved in some wheezing syndromes.

Several other investigations have demonstrated that chronic respiratory symptoms in children, including the occurrence of wheeze, are reported more frequently in the children of parents who smoke cigarettes (31-38). Several of these studies have observed that the prevalence of wheeze in children was higher for those children whose parents also wheeze (31, 32, 39). However, the trend of increased wheezing with increasing parental smoking observed in our study children has been shown to be independent of parental history of wheezing, since a significant trend of similar magnitude persists when the analysis is restricted to nonwheezing parents of either sex. These data suggested, therefore, that exposure to parental cigarette smoke in our population is related to the occurrence of wheeze in children.

All of the children included in the present report were included in a previous study that demonstrated an inverse relation between the degree of $FEF_{25-75\%}$ in children and the amount of parental smoking (19). Although we have restricted the present analysis to the youngest children in the overall study population, the effects of parental smoking on pulmonary function were similar in magnitude to those obtained when children 19 yr of age or younger were included in the analyses. This indicated that the effects of parental smoking could be measured early in life and were not, in fact, substantially dependent upon significant smoking by the children themselves.

Regression analysis was used to identify how factors such as parental smoking, children's own smoking, and the occurrence of wheeze affected the FEF-Z scores. Although the r^2 for the overall model was small (0.08), several interesting observations emerged from this analysis. Despite the fact that the presence of persistent wheeze was associated with lower FEF-Z scores (table 6), the mother's current smoking history was the most significant overall predictor of a lower FEF-Z score (table 8). This observation was consistent with an earlier study in this community (using a different sample of children) that also demonstrated that the mother's smoking history was a significant predictor of FEV_1, expressed as a per cent of predicted value (40). Similarly, Hasselblad and colleagues (41), in a study of 16,686 white children 6 to 14 yr of age, observed that, after age, height, and sex, the mother's current smoking (measured as packs per day) was the most significant predictor of the degree of FEV_1. Although these observations stress the importance of the most recent smoking experience of the mothers, the possibility also remained that smoking during gestation and the neonatal period may also have contributed to altered lung function. No satisfactory data are available concerning this early age group.

The failure to find that the father's smoking was a significant predictor of the degree of function in this and the other 2 studies cited would, at first glance, appear to contradict the observation of an inverse linear trend between the FEF-Z score and the number of parents smoking (19) (table 7). However, most of the effect in the trend analysis was between the households in which neither parent was a current smoker and households in which 1 parent was a current smoker. Differences between households where one and those where both parents smoked were less striking. Further analyses, particularly of the relation between rate of change of function with growth and parental smoking, are being undertaken to try to determine how these associations change with time.

The finding that the child's own smoking habits were not a significant predictor of the degree of function was in sharp contrast to previous work in this population in which these children were included (19). However, the prior analysis included children as old as 19 yr of age, whereas this analysis was restricted to those 5 to 10 yr of age. The number of smokers in this age group was quite small (table 5). Furthermore, those children who did report having smoked, smoked infrequently, usually less than 1 cigarette per week. Thus, for this age group, personal smoking did not occur often enough or with enough intensity to be a significant predictor of FEF-Z score.

The fact that the regression analysis identified the mother's smoking history as a stronger predictor of FEF-Z score than the symptom of persistent wheeze would suggest that the lower FEF-Z scores observed in the children of smoking parents was not simply a function of the fact that these children had a tendency to wheeze, and, therefore, would be more likely to experience episodes of subclinical bronchoconstriction at the time they were asked to perform the FVC maneuvers. The identification of persistent wheeze as the second strongest predictor of FEF-Z scores was open to several interpretations because of the cross-sectional nature of the data. Thus, it was equally likely that the presence of wheeze identified a group of children for whom wheeze was an additional marker for stable deficits in function and/or a group of children with transiently lowered degrees of function due to bronchomotor hyperreactivity.

A number of children had to be excluded from several of the analyses because of missing data. The possibility that these exclusions might have led to bias in the relation between persistent wheeze and the parental smoking and pulmonary function variables was explored. Children who were excluded were significantly younger and were significantly less likely to have ever smoked cigarettes than those included in the various analyses, but were not significantly different in their reported prevalence of current persistent wheeze. Furthermore, these excluded children were similar to those included in the analyses with regard to a number of demographic variables including the parental smoking histories, which might have influenced the reported relationships. Thus, it seems unlikely that differences between children included and not included in the analyses could explain the observations reported.

Existing data concerning the possible mechanisms by which passive exposure to cigarette smoke might lead to the occurrence of persistent wheezing are few, but a direct irritant and/or immunologic effect is possible (42). Similarly, lower respiratory illnesses might be influencing the occurrence of wheezing by either of these mechanisms (43).

The association of current persistent wheeze in children with a history of atopy, respiratory illness, and parental cigarette smoking to a lower degree of pulmonary function in children suggested that factors acting in childhood may be directly relevant to the subsequent risk of developing obstructive airway disease in adult life. The prospective test of this hypothesis remains the central goal of the study from which the present data have been derived.

Acknowledgment

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Comparisons were made between children living in homes with gas
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small but significantly lower levels of FEV1 and FVC corrected for
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findings were not explained by differences in social class or by
parental smoking habits. Measurements taken in the homes for 24-h
periods showed that NO2 levels were 4 to 7 times higher in homes
with gas stoves than in homes with electric stoves. However, these
24-h measurements were generally well below the current federal
24-h outdoor standard of 100 ug/m3. Short-term peak exposures,
which were in excess of 1,100 ug/m3, regularly occurred in kitchens.
Further work will be required to determine the importance of these
short-term peaks in explaining the effects noted.

Respiratory Disease Rates and Pulmonary Function in Children Associated with NO₂ Exposure[1-4]

FRANK E. SPEIZER, BENJAMIN FERRIS, JR., YVONNE M. M. BISHOP, and JOHN SPENGLER

SUMMARY

As part of a long-range, prospective study of the health effects of air pollution, approximately 8,000 children from 6 yrs to 10 yrs of age from 6 communities had questionnaires completed by their parents and had simple spirometry performed in school. Comparisons were made between children living in homes with gas stoves and those living in homes with electric stoves. Children from households with gas stoves had a greater history of respiratory illness before age 2 (average difference, 32.5/1,000 children) and small but significantly lower levels of FEV₁ and FVC corrected for height (average difference, 16 ml and 18 ml, respectively). These findings were not explained by differences in social class or by parental smoking habits. Measurements taken in the homes for 24-h periods showed that NO₂ levels were 4 to 7 times higher in homes with gas stoves than in homes with electric stoves. However, these 24-h measurements were generally well below the current federal 24-h outdoor standard of 100 μg/m³. Short-term peak exposures, which were in excess of 1,100 μg/m³, regularly occurred in kitchens. Further work will be required to determine the importance of these short-term peaks in explaining the effects noted.

Introduction

There is little doubt that NO₂ at high concentration is associated with acute pulmonary edema and death. Silo filler's disease in which farmers are exposed to concentrations of NO₂ in excess of 200 ppm (376,000 μg/m³) with a resultant occurrence of acute pulmonary disease and occasionally death was described in the 1950s (1). Farmers surviving such exposures can develop pulmonary fibrosis.

Recently, concern over the effects of indoor exposure to lesser concentrations of NO₂, both repeated short-term peak exposure and continuous low exposure, has led to studies of children (2) and housewives (3) but with inconsistent results. Melia and co-workers (2) from Great Britain reported higher rates of lower respiratory disease in school children living in households with gas cooking stoves than in those living in households with electric stoves. These differences in rates could not be explained by social class or differences in household size. However, this study did not take into account the smoking habits of the parents of these children. Subsequently, Melia and co-workers (4) found that households with gas cooking stoves had 7 times higher concentrations of NO₂ in the kitchen than did matched households with electric cooking devices. Similar studies in the United States found concentrations

of NO, 4 times greater in kitchens of households with gas stoves than in those with electric stoves (5). The NO, appears to be produced by the oxidation of NO when natural gas as a fuel for cooking is burned in the atmosphere. The conversion is rapid, and the NO, spreads quickly throughout the house. In contrast to the Melia study of children (2), a study of adult women living and working in households with gas stoves compared with those living and working in households with electric stoves did not show increased respiratory disease rates (3).

The results reported here were obtained as part of a long-range prospective study on the health effects of exposure to ambient levels of pollutants resulting from the burning of fossil fuels. In this study, adults between the ages of 25 and 74, selected at random from 6 communities in the eastern United States, are seen every 3 years, and school children (initially seen in grades 1 and 2) are seen annually. This report is based on the initial measurements of pulmonary function and information on respiratory diseases obtained in the children only in the 6 cities and relates these measurements to the potential indoor exposure that these children have received.

Methods

Study design. A total of 9,280 children participated in the initial surveys. These children represented 12 separate cohorts from 6 cities. Two cities were surveyed for 3 years, and a new group of first-grade school children was added each year. Thus, these cities provided 6 cohorts. Two cities were surveyed for 2 years giving 4 more cohorts, and 2 cities were surveyed once. In all the cohorts, more than 95 % of the children eligible because of their school grade were studied.

Information about the children's exposure was obtained from a questionnaire, completed by their parents, on the type of home-cooking device and home-heating fuel, the presence or absence of air conditioning, and the presence or absence of adult smokers living in the household, as well as requesting permission to perform lung function tests on the children in the schools.

Forced expiratory measurements were performed using a water-filled low-inertia recording spirometer. The children did not wear nose clips and performed the task in a sitting position, but with free movement possible. Each child had a minimum of 5 and a maximum of 8 attempts in an effort to obtain at least 3 acceptable tracings. Forced vital capacity (FVC) and forced expiratory volume in 1 second (FEV,) were read from each tracing. Values were corrected to body temperature and pressure saturated with water vapor (BTPS) and summarized as the mean of the 3 best efforts that were within 170 ml of each other. Standing height in stockinged feet and weight were recorded for each child.

There were 8,866 children (95.5 % of the total seen) who were between 6 yrs and 10 yrs of age at the time of their initial survey, but the sample was reduced to 8,120 children by limiting the analyses to white children.

For each child included in the study, the lung function predicted for his or her height was computed from a regression equation determined by using the children studied in the third year of follow-up from 2 of the cities. These children, who were all within the 5 to 95 percentiles for their height corrected for age, were chosen for the standard as they provided sufficient numbers at each year of age between 6 yrs and 10 yrs (6). The difference between the observed lung function and the predicted value was obtained. These residuals were analyzed using standard analysis of variance techniques.

The reported disease rates were analyzed using log-linear models. By this means it was possible to determine significant interactions between disease, age, sex, cohort, city, and home variables. Adjusted rates were computed based on models that included the significant interactions (7).

Information regarding the differences in air quality associated with different cooking devices was obtained by setting up indoor-outdoor monitors in selected households. These households were not necessarily the homes of children in the study, but were selected to be representative of the kinds of living patterns found in each community. The homes were sampled every sixth day for 24 h, and the same time period in each city, May 1977 through April 1978, was used in all analyses. Measurements were carried out by a household sampling unit, which was placed in an "activity room," a room specifically defined as not being the kitchen or bedroom. Mass respirable particulates (mass median diameter of 3.5 μm) were collected on millipore filters (8), and NO, was collected by a bubbler technique and measured by the EPA Reference Method, a modified sodium arsenite method (9).

The data on air pollution levels were first adjusted to take into account missing values using a linear model for day of observation and site. The influence of home variables was determined by analysis of variance, with appropriate adjustment of the residual degrees of freedom. In one household, instantaneous peak levels of NO, were monitored in the kitchen within 3 feet of a gas stove using a chemiluminescence monitor and a continuous recording.

Results

Assessment of exposure to NO,. About half of the homes in all 6 cities had gas cooking stoves, and about half had electric cooking stoves. (Six % of the homes used some other form of cooking device, alone or in conjunction with gas and/or electricity [1.9 %], or else the type of cooking device was not reported [4.1 %].) There were, however, considerable differences between cities (figure 1). The distribution of the children by home cooking device ranged from a high of 82.2 % gas cooking
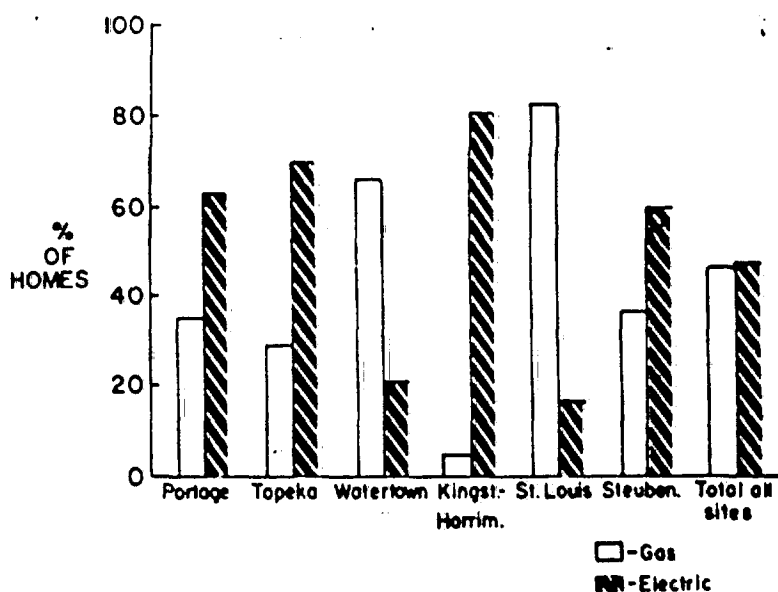
Fig. 1. Percentage of homes with gas or electric stoves, by cities.

stoves in St. Louis to a low of 4.6 % in Kingston-Harriman (figure 1).

Although the number of homes where air quality measurements were made is not large, ranging between 5 and 11 for different cities, the number of 24-h periods for which matched indoor and outdoor data are available is several hundred (table 1). The homes were divided between gas and electric cooking devices, except for Kingston-Harriman where no homes with gas stoves were studied. The results show a gradient of NO_2 levels in homes with electric stoves that reflect outdoor sources of NO_2. High concentrations in Watertown were presumed to be caused by the proximity of homes, and therefore the monitors, to automobile traffic. A substantial increase in NO_2 levels in homes with gas stoves, except for Steubenville, reflects the addition of indoor sources to the outdoor level of NO_2. These are 24-h integrated averages collected in an "activity room," but not in the kitchen. In some cities the daily 24-h levels encountered in some households with gas stoves exceeded the federal standard for the annual average of the 24-h NO_2 levels ($100\,\mu g/m^3$). Such levels for integrated 24-h values indicated that peak exposures must be substantially higher. This was confirmed in 1 household in which instantaneous monitoring in the kitchen produced peak levels over $1,100\,\mu g/m^3$ for short periods of time when the oven was in use and peaks over $500\,\mu g/m^3$ when a single gas burner was on (figure 2).

Health data. Two sets of data on the children's

health were available: data on previous illnesses reported on questionnaires completed by parents, and data from the current pulmonary function tests. The responses to 3 questions about the previous health of the children were analyzed. The questions asked if there was a history of bronchitis diagnosed by a physician, a history of serious respiratory disease before age 2, and a history of a respiratory illness in the last year.

Both the responses to these questions and the pulmonary function measurements were tested for their relationship to several household variables: type of cooking device, nature of fuel used for heating, presence of adult smokers, presence of air conditioning, and socio-economic status of the family. Socio-economic status included both occupation and educational attainment of the parents.

The 3 reported disease rates were analyzed by fitting log-linear models (7). Two of the variables, type of home-heating fuel and air conditioning, were not related to the disease rates. The social class, parental smoking, and type of cooking stove variables had differing effects on the 3 diseases when each home variable was tested alone (table 2). As the risk factors themselves were interrelated, each disease was evaluated in another log-linear analysis that included these 3 home variables simultaneously. In this multivariate analysis, the effect of the type of cooking stove had a significant association with respiratory disease before age 2, but not with the other 2 reported dis-

TABLE 1

INDOOR AND OUTDOOR 24-H LEVELS OF NO₂ IN 6 U.S. CITIES
(MAY 1977 TO APRIL 1978)

| City | Home Cooking Units | | | Geometric Mean Level of NO₂ ($\mu g/m^3$) | | | | 95 Percentile Measured Level of NO₂ ($\mu g/m^3$) | | | |
| | Days (no.) | Electric (no.) | Gas (no.) | Outdoor | | Indoor | | Outdoor | | Indoor | |
				Electric	Gas	Electric	Gas	Electric	Gas	Electric	Gas
Portage*	50	8	3	7.2 (1.55)	5.9 (1.10)	3.6 (2.13)	14.7 (1.02)	31.8	25.4	17.6	39.3
Topeka	57	6	1	17.5 (1.25)	18.2 —	19.4 (1.26)	31.6 —	42.4	40.7	41.6	73.6
Kingston-Harriman	56	8	—	17.2 (1.25)	—	10.9 (1.43)	—	38.4	—	29.8	—
St. Louis	58	3	8	33.0 (1.17)	37.3 (1.14)	17.1 (2.01)	40.8 (1.42)	84.3	70.9	83.3	79.3
Steubenville	61	2	3	35.7 (1.00)	33.3 (1.35)	21.9 (2.59)	27.4 (2.24)	82.9	87.8	74.5	103.9
Watertown	59	2	5	49.1 (1.42)	49.2 (1.10)	41.43 (1.14)	54.3 (1.21)	101.6	106.3	95.2	118.3

* Based on 10-month sample.
† Federal 24-H standard = 100 $\mu g/m^3$.
‡ Numbers in parentheses are geometric standard deviations.

cases (table 3). Parental smoking, sex of the child, and city-cohort, but not age at the time of reporting were also associated with respiratory disease before age 2 when other variables were taken into account. Disease rates adjusted for parental smoking, social class, and city-cohort resulted in a difference of 35/1,000 among males and 30/1,000 among females between children in homes with different cooking stoves. Lower rates were found in children of households with electric stoves for each sex in each city-cohort adjusted for parental smoking and social class (figure 3). The effects of parental smoking and city-cohort on respiratory disease before age 2 are not independent, but the effect of the type of cooking stove appeared to be related to the other home variables.

To assess the effect of home factors on pulmonary function in these children, the difference between the expected and observed FVC and FEV₁ was calculated for each child. The effect of cohort (yr of study and city) and the same home variables on the residual pulmonary function were assessed by analysis of variance. Preliminary regression of lung function on socio-economic status showed no relationship. There was a significant effect ($p < .01$) of cohort on both FEV₁ and FVC. Thus, from city to city and from year to year there were differences in the height-adjusted pulmonary
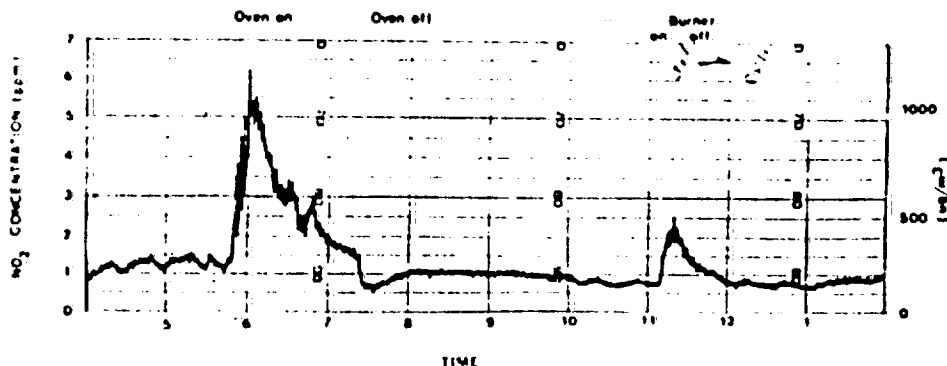

Fig. 2 Instantaneous monitoring of NO₂ in the kitchen 1 meter from gas stove. Numbers along the abscissa represent hrs in the day through 1 A.M. No venting was used.

TABLE 2

SINGLE FACTOR ODD RATIOS (OR) AND 95% CONFIDENCE LIMITS (CL)
FOR HOME VARIABLES AND REPORTED DISEASE RATES

		Social Class (Low/High)	Parental Smoking (Some/None)	Home Cooking (Gas/Electric)
History of doctor-diagnosed bronchitis	OR	0.97	1.08	0.85
	CL	.86-1.08	.94-1.26	.79-0.91
Serious respiratory illness before age 2	OR	1.13	1.32	1.12
	CL	1.01-1.26	1.12-1.57	1.00-1.26
Respiratory illness in the last year	OR	1.13	1.19	0.94
	CL	1.05-1.22	1.02-1.39	.84-1.85

function levels in these children, after adjusting for city-cohort effects. There were no significant associations between the presence of air conditioning in the home and lung function measurements (table 4). Although the association between parental smoking and FVC was significant at the 5% level, with an average range of 15 ml, the result was the opposite of that anticipated, and there was no association between FEV₁ and parental smoking. Home heating and FEV₁ residuals were also significantly associated at the 5% level. The over-all means covered a 28-ml range and the ordering from low to high was oil, gas, electric.

Although FEV₁ residuals were affected by home heating fuels, the most consistent and significant finding was the lower levels of both FVC and FEV₁ in children whose homes had gas cooking stoves compared with those whose homes had electric stoves. The over-all effect of home cooking, after correcting for cohort effect, was 16 ml and 18 ml, respectively, for FEV₁ and FVC. This effect is apparent in almost all the cohorts. For FEV₁, in 10 of 12 cohorts, the children in homes with gas stoves had lower function than children in homes with electric stoves (figure 4). For FVC, only 1 of the cohorts (St. Louis, first year), did not show lower levels of pulmonary function in children living in homes with gas stoves compared with those living in homes with electric stoves (figure 4). An unexpected finding in these data

was the low level of pulmonary function measured in Topeka, which is a city with generally lower levels of ambient pollution. In an attempt to investigate this finding, we tested the effect of different interviewers, we reread the spirometer tracings to test the effect of readers, and we compared the values obtained on each spirometer by month of study to test the possibility of a defective machine. None of these tests explained the lower pulmonary function values. In addition, the distribution of height for age of the children in Topeka did not differ significantly from the other cities. We were thus left with the observation that the pulmonary function measurements in the children in Topeka were lower than in other cities and must assume that it was a cohort effect needing further study.

Discussion

The significant associations found in this analysis were between home cooking stoves and both illness history and lung function. In addition, there was an association between parental smoking and disease history. The importance of these findings rests with the interpretations of these significant, albeit relatively small, changes. Sufficiently large groups are being studied to observe minor differences between them. The size of the differences found was consistent with the anticipated magni-

TABLE 3

VALUES OF G* FOR SPECIFIED DISEASE RATES FOR EACH HOME VARIABLE
AFTER ADJUSTING FOR THE OTHER TWO HOME VARIABLES

	Social Class		Parental Smoking		Home Cooking	
	G*	P	G*	P	G*	P
History of doctor-diagnosed bronchitis	0.70	NS	1.10	NS	1.90	NS
Serious respiratory illness before age 2	4.12	<.05	10.21	<.01	6.70	<.01
Respiratory illness in the last year	2.12	NS	4.38	<.05	0.14	NS

* G* is a likelihood statistic derived from the log-linear analyses and is distributed, in each case, like a chi square with 1 degree of freedom.

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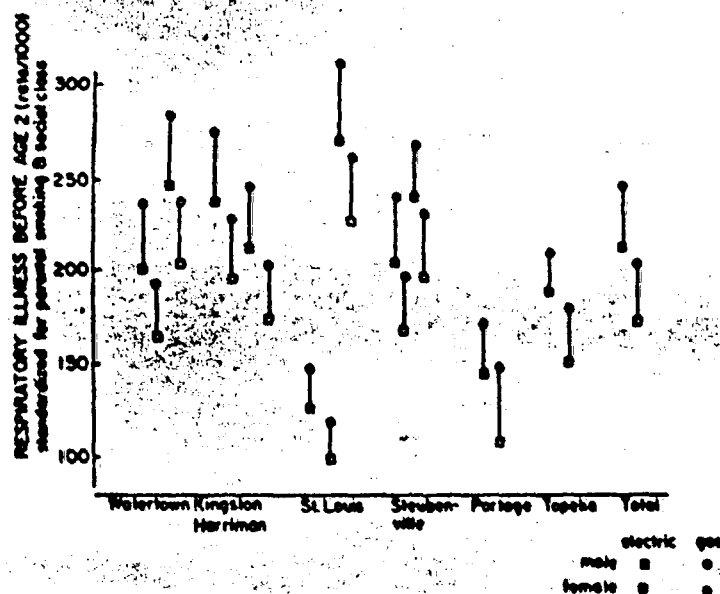
Fig. 3. Respiratory illness before age 2 standardized for parental smoking and social class by cohorts in children 6 to 10 yrs old. Males and females separately by cohort and gas or electric stoves.

tude of effect of environmental agents (11), and the home measurements of air quality are supportive.

The evidence that homes with gas cooking stoves have higher levels of NO_2 than similar homes with electric stoves has been demonstrated a number of times (4, 5), and peak levels measured over gas stoves have on occasion been reported to reach approximately 1 ppm (1,880 $\mu g/m^3$) for periods of 10 to 15 min. This was confirmed in 1 household during continuous monitoring. Similarly we know from both our own investigation and from the studies of Hinds and associates (12) that the mass respirable particulate loads in households with smokers can be severalfold higher than in nonsmoking households.

TABLE 4

ANALYSIS OF VARIANCE OF CHILDREN'S LUNG FUNCTION FOR HOME VARIABLES
(CITY-COHORT ADJUSTED)*

Home Variable	Children (no.)	Lung Function Residuals			
		FEV_1 (liter)	F Ratio	FVC (liter)	F Ratio
Cooking fuel	6,803	—	—	—	—
gas	3,274	−.008	8.11†	−.009	7.94†
electric	3,529	+.008		+.009	
Home fuel	6,734				
oil	1,419	−.011		−.005	
gas	4,432	+.001	3.26†	−.005	0.76
electric	883	+.017		+.010	
Air conditioning	7,126	—		—	
none	2,855	−.001		−.002	
partial	2,363	+.003	0.61	+.006	1.22
central	1,908	−.003		−.004	
Parental smoking	5,842	—		—	
none	1,724	−.001	.03	−.011	6.26†
some	4,118	+.000		+.004	

* See text for definition of different cohorts. Largest cohort home variable interaction terms gave F ratio of 1.3, not significant.
† $p < .01$
‡ $p < .05$

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Fig. 4. Forced expiratory volume in 1 s and forced vital capacity residuals by cohort and gas and electric stoves in children 6 to 10 yrs old. (Numbers under the FEV₁ values are the same for FVC values.)

Other factors affecting the association between the disease and either the presence of gas stoves or smoking in the household seem to have been excluded (e.g., socio-economic status, presence of air conditioning, and the type of heating fuel).
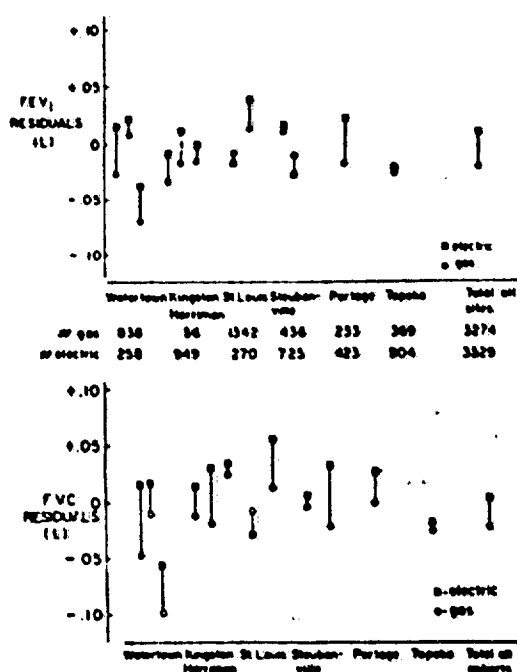
In considering the importance of these findings, a number of potential sources of bias must be evaluated. The questionnaire information on disease rates for an individual child depends on the recall ability of the parents, and it may be biased by the present status of the child. The responses also may be biased by the parents' lack of knowledge. No attempt was made to have doctor confirmation of diagnosed disease confirmed independently. It seems unlikely, however, that any biases introduced by these means would be related to the type of home cooking stove consistently for each city and each cohort.

The good response rate, and the sampling plan that ensures that all potentially available children are seen means that the samples are representative of the cities.

The pulmonary function data are potentially subject to different sources of bias than the questionnaire data. These include possible interviewer bias, malfunctioning machine, and biased reading of the spirometer tracing. All these sources of bias have been looked for and have not been found. In

any case, neither the field screeners nor the readers were aware of the individual child's home environment when the spirometry was performed or when the tracings were read. Thus, we cannot attribute any bias to association with home variables.

Essentially, the interpretation of the pulmonary function finding relates to the sensitivity of the measurement and the biologic expectation of the magnitude of anticipated effect in a group of children between 6 yrs and 10 yrs of age. We used FEV₁ as a measure of air flow obstruction in these children, not because we believed it to be the best measure of early obstruction, but because our plan is to follow these children over several years. After several years they will be at a point at which a stable estimate of change in pulmonary function can be related to our understanding of the development of adult obstructive airways disease. In these children, many of whom can empty their entire FVC in less than 2 s, the FEV₁ does not measure obstruction as much as it measures FVC. Thus, it is reassuring to find similar changes in both measures when trying to understand the significance of any given finding.

Our understanding of the biology of lung growth and the nature of the onset of obstructive lung disease in adult life lead us to believe that only minor difference in the rate of functioning lung growth in young children could lead to these children not reaching their full adult lung size. (We are using FVC as a crude indicator of lung size recognizing that the TLC includes not only FVC but also the residual volume, which is not being measured in these field studies.) We do not know whether failure to reach full adult lung size is related to the subsequent susceptibility of developing obstructive lung disease, but it is not an untenable hypothesis that those persons with minor impairment of total lung growth are more susceptible to rapid decline in pulmonary function in adult life (13).

These results differed from those reported in the literature to date only in modest ways. The findings of Melia and co-workers (2) regarding lower respiratory tract illness rates in children whose homes have gas stoves were similar. That study was criticized because it did not have smoking data. In this study the adjustment of rates of illness before age 2 for smoking led to a clear association with gas cooking devices; however, the adjustment of the other 2 historical disease indicators reduced the associations found. The study of Keller and associates (14) of both adults and children in a selected sample of households suggest no association of gas stoves with respira-

tory disease rates. This study measured incidence of acute respiratory disease over the course of 1 year; but the number of children studied was quite small and clearly did not represent a general population. Bouhuys and co-workers (15) did study population-based samples of children and adults, but out of the 7,000 persons studied only 165 children between the ages of 7 yrs and 14 yrs were included from the 2 communities under investigation (16). Thus, the fact that they were unable to find an association with home cooking devices may be attributed to the small number studied.

Tager and associates (17), using a different indicator of airways obstruction (mid-maximum expiratory flow), found an association between the pulmonary function levels in children and the number of smokers in the household. No such association using FEV₁ was found in this study. This may mean that the airways obstruction measurement was insensitive.

Further follow-up of these cohorts are underway. Because these data deal with retrospective information, the initial findings reported here need replication to ensure that some subtle bias or alternative explanation for the findings has not been overlooked. If the relative position of these children's lung sizes changes on repeated assessment, it will be important to assess the factors that influence the change. These factors may include changes in ambient pollution (outdoor levels) or changes in personal pollution (indoor exposures and cigarette smoking). In addition, other personal factors such as frequency of respiratory infections, familial history of disease, or other recognized potential risk factors for developing chronic obstructive respiratory disease not discussed in this report will need to be considered.

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SUMMARY: Using pulmonary function and family respiratory questionnaire data for 16,689 white children 8 to 13 yr of age from 7 geographic areas, the investigators examined the effect of several environmental and other factors on performance in a standard test of breathing. As expected, FEV.75 was correlated most strongly with age, height, and sex.   A dose-response relationship was observed with maternal smoking habits and explained 0.1% of the variance.   No effect caused by the father's smoking habits was observed.   A decrease (p = 0.0524) in FEV among older girls was associated with the presence of a gas cooking stove in the home. Although the statistical significance of the decreases was largely attributable to the size of the sample, the decreases in FEV, even though small, were thought to be biologically significant.

Indoor Environmental Determinants of Lung Function in Children[1,2]

VICTOR HASSELBLAD, CHARLES G. HUMBLE, MORGAN G. GRAHAM and HELEN S. ANDERSON

Introduction

Lung function in children has been related to both genetic and environmental factors. Genetic factors exert the greatest influence through general stature, as measured by height and by age. Environmental exposures include both those ambient in origin and those attributable to indoor sources such as smokers and gas stoves. This report discusses the association of indoor environmental pollutants and children's lung function.

It is well known that familial factors are important predictors of respiratory disease (1-6). Investigators have observed an excess prevalence of chronic bronchitis in relatives of persons with bronchitis when compared with relatives of persons without bronchitis (1-3). More recent studies have noted the household clustering of bronchitis and described its genetic component (4-6).

Genes, however, are only one thing that a family has in common; a large amount of time spent breathing a common atmosphere is another. Estimates vary, but children living in a temperate zone are thought to spend 60 to 80% of their time indoors on an average school day (7). Thus the presence of known sources of pollution (e.g., smokers and gas stoves) inside the home where reduced ventilation can lead to pollutant build-up may expose children to potentially harmful environments.

The impact of smoking on indoor atmospheres has been demonstrated numerous times (7-9). For example, under average indoor conditions, concentrations of particles in the respirable range (<3.5 microns in diameter) can exceed the National Ambient Air Quality Standard for total suspended particulates (all particles <30 microns in diameter) (9).

Several studies have reported that exposure of infants to side-stream smoke from parental smoking increases the risk of an attack of pneumonia or bronchitis (10-12), but this association was not observed in children 1 to 5 yr of age. Speizer and co-workers (13) found an association between parental smoking and a history of respiratory disease in children younger than 2 yr of age. Colley (14) reported that the prevalence of cough in children 6 to 14 yr of age was associated with their parents' smoking habits and that the prevalence was highest when both parents smoked and lowest when neither parent smoked.

The literature regarding effects of passive smoking on lung function is limited. Leeder and associates (15) observed no influence of parental smoking habits on peak expiratory flow rates of children 0 to 5 yr of age, even though parental smoking was associated with the incidence of bronchitis in the first year of life. In the same cohort, bronchitis in the first year of life was associated with decreased expiratory flow rates. By contrast, Tager and colleagues (16) recently reported that children 5 to 19 yr of age showed patterns of decline in forced expiratory flow during the middle half of the FVC ($FEF_{25-75\%}$) that were indicative of a dose-response relationship with parental smoking. However, no association of parental smoking with respiratory illness was observed in these children.

In addition to passive smoking, the health significance of the gas-fueled stove is also becoming apparent. Numerous studies have demonstrated that gas stoves contribute significantly to indoor nitrogen dioxide concentrations (17-21). Although experiments involving animals have suggested an association between nitrogen dioxide and respiratory infections (22-24), the epidemiologic evidence does not disclose a consistent relationship between NO_2 exposure from gas stoves and health effects. Melia and co-workers (25) conducted a longitudinal study examining the relationship of cooking fuel and respiratory disease in children. They concluded that girls from homes using gas for cooking reported more respiratory symptoms or diseases than were reported by girls from homes where electricity was used. Speizer and co-workers (13) found children 6 to 10 yr of age in homes equipped with a gas stove to have significantly lower FEV_1 and FVC values and to have a greater history of respiratory illness before 2 yr of age, when compared with children of the same age in homes with electric stoves. By contrast, Keller and colleagues (26) compared gas and electric cohorts of school-age children. The data revealed no differences in reported incidence of respiratory illnesses, the frequency of symptoms, or the fre-

SUMMARY. Using pulmonary function and family respiratory questionnaire data for 16,689 white children 6 to 13 yr of age from 7 geographic areas, the investigators examined the effect of several environmental and other factors on performance in a standard test of breathing. As expected, $FEV_{0.75}$ was correlated most strongly with age, height, and sex. A dose-response relationship was observed with maternal smoking habits and explained 0.1% of the variance. No effect caused by the father's smoking habits was observed. A decrease (p = 0.0524) in FEV among older girls was associated with the presence of a gas cooking stove in the home. Although the statistical significance of the decreases was largely attributable to the size of the sample, the decreases in FEV, even though small, were thought to be biologically significant.

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quency of positive respiratory findings on physical examination.

Methods

The data for this study were collected between 1970 and 1973 as part of the Environmental Protection Agency's Community Health Environmental Surveillance System (27). We were careful to select for this report only data that were comparable with those in the existing epidemiologic literature. Potential methodological problems in the data are discussed where needed.

Community selection. Communities were chosen from 7 metropolitan areas in different geographical regions of the continental United States (table 1). Ambient air pollution measurements were obtained from 1971 to 1973, which provided data for total suspended particulates, respirable suspended particulates, and the water-soluble sulfate fraction of the total suspended particulates. Monitoring of indoor atmosphere was not a part of this program, but relative exposures

to NO_2, total suspended particulates, and respirable suspended particulates can be inferred from the presence or absence of gas stoves (19-21, 26) or smokers (7, 28, 29) in the house.

Questionnaire administration. Within each community, children in the elementary schools (5 to 13 yr of age) were enrolled (table 1). A family health questionnaire, based on the British Medical Research Council's Chronic Bronchitis questionnaire, was distributed via the youngest child from each family. From this questionnaire, current parental smoking habits, family socioeconomic status, and other information were obtained (27). Where possible the mother or female guardian was asked to complete the form and return it to the school for collection. In all areas except Utah, questions regarding the nature of cooking and heating in the home were asked. For the children recruited, data on personal smoking habits and respiratory illness histories (other than asthma) were not collected.

Questionnaire distribution covered a 2-yr

period with pulmonary function testing taking place during the 1972-1973 school year. The questionnaire data was at times collected in advance of the testing (for exact distribution dates, see table 1). In New Jersey, for example, questionnaires were distributed between 15 and 24 months prior to pulmonary function testing. Parental cooperation, averaged over all areas, was approximately 85%.

Pulmonary Function Testing. Pulmonary function testing was performed in the schools with a 12-L bellows-type spirometer manufactured by Cardiopulmonary Instruments, Inc. (Houston, Texas). In this instrument, expired air displaces a cylinder whose air seal is a pliable rolling diaphragm. The mechanical displacement of the piston over 0.75 s was transduced to a voltage that was displayed as $FEV_{0.75}$ (forced expiratory volume in 0.75 seconds) on a nixie-tube digital readout.

The study design allowed for only $FEV_{0.75}$ measurements to be obtained. Using the digital display of the $FEV_{0.75}$ precluded the

TABLE 1
SAMPLE SIZES, DATES, AND EXCLUSIONS BY COMMUNITY

Community	Original Number Surveyed	Number Nonwhite	Number Asthmatics	Number with <2 Tests*	Number with No Background Information	Number with Complete Information on Both Parents	Dates of Background Questionnaire
Charlotte NC							
Sector 2	2,605	1,066	77	504	332	556	10/72-12/72
Sector 3	2,524	954	82	569	402	441	10/72-12/72
Sector 4	2,301	754	55	522	92	771	10/72-12/72
Birmingham AL							
Inglenook	1,270	189	72	389	121	458	10/72-12/72
Norwood	2,062	1,879	13	87	30	44	10/72-12/72
Zion City	1,008	221	56	262	148	279	10/72-12/72
Center Point	1,994	225	75	448	60	1,118	10/72-12/72
Homewood	1,412	155	69	341	33	895	10/72-12/72
Hueytown	1,722	285	110	403	61	796	10/72-12/72
Riverhead NY	1,402	496	35	322	187	309	5/72
Queens NY	1,272	103	41	531	157	411	5/72
Bronx NY	1,324	309	34	410	204	318	5/72
Sheepshead Bay NY	1,003	124	32	305	125	361	5/72
Ridgewood NJ	1,434	58	41	473	282	554	6/71
Fair Lawn NJ	1,270	27	40	419	210	549	6/71
Matawan NJ	1,385	35	51	439	259	582	6/71
Elizabeth NJ	1,372	176	30	450	181	464	6/71
Ogden UT	1,259	120	42	389	440	239	12/70
Salt Lake City UT	1,971	340	57	642	480	377	12/70
Kearns UT	2,007	167	73	734	505	485	12/70
Magna UT	2,052	244	69	576	476	619	12/70
Chattanooga TN							
Red Bank	1,878	10	65	594	607	551	1/72-3/72
Brainerd	2,146	686	65	469	425	432	1/72-3/72
Harrison	2,125	206	61	622	618	571	1/72-3/72
Vista CA	2,479	573	138	512	434	736	12/71-3/72
Santa Monica CA	2,295	587	138	498	412	472	12/71-3/72
Anaheim CA	2,555	271	180	663	591	726	12/71-3/72
Glendora CA	2,245	125	160	540	496	865	12/71-3/72
Thousand Oaks CA	1,902	106	131	535	374	712	4/72-5/72
Garden Grove CA	2,180	284	136	654	409	593	4/72-5/72
Covina CA	2,414	378	151	686	501	605	4/72-5/72
Total	56,868	11,153	2,379	14,964	9,652	16,689	

* Includes those absent or those present with cough, cold, or sore throat, twice or more

correction of each reading for submaximal effort at the beginning of a test. The values reported here are actually for FEV of less than 0.75 s. The average amount of time less than 0.75 s and the reduction of air volume associated with it were unobtainable from our data.

The cardiopulmonary instrument was calibrated before testing each day against both a Collins water-filled spirometer and a 1.5-L syringe. Several times each testing day the linearity of the digital readout was checked. To counter potential technician differences, an average of all blows from more than one period was taken. All raw $FEV_{0.75}$ readings were converted to body temperature and pressure-saturated conditions (BTPS). Different technicians and machines were used in each metropolitan area.

Pulmonary function testing was conducted seasonally during the school year for a different number of years in each area (table 1). To control for possible annual differences in testing procedures, only tests from the 1972-1973 school year have been used in the following analyses. Three rounds of tests were conducted that year: fall 1972, winter and spring 1973. Just before testing, the children received an introduction and test demonstration that emphasized maximal inspiration first, then expiration, as forceful and complete as possible, into the spirometer. Each child was tested until 3 acceptable FEV measurements were obtained. The maximum of each child's 3 readings was used in the data analysis. At the time of testing, each child reported the presence or absence of a cough, cold, or sore throat.

Each technician was responsible for selecting an acceptable test. To check technician selection accuracy, an average was taken of each technician's 3 (acceptable) recorded FEV values. All means obtained for each day of testing were averaged for every technician. The technician supervisor was to correct any technician who consistently produced a mean score that differed from the mean scores of other technicians.

Sample selection. The original file contained 56,864 children who participated at any time in the 1972-1973 school year (table 1). To avoid possible confounding by race (28), analyses were restricted to the 45,711 white children. Any child reported to have ever had asthma was excluded. Only children free of respiratory symptoms in at least 2 test periods were included. This left 28,366 children eligible for analysis.

In order to investigate the association of parent-reported socioeconomic and exposure information with FEV values, it was necessary first to link the parents' questionnaire information to the data from the children's pulmonary function tests. This proved to be difficult. Although there were problems with record keeping, most of the difficulty was attributable to the interval between questionnaire distribution and pulmonary function testing. As a result of this interval, linkage was not possible for those eligible

who had moved out of study communities (after questionnaire distribution but before testing) and those eligible who had advanced to an age that disqualified them from participating. The average linkage achieved for all areas was approximately 65%, which reduced the sample to 18,716. The sample was further reduced by restricting the analysis to students for whom smoking information on both parents was available. The final sample total, then, included 12,748 families with 16,689 white, symptom-free children tested in at least 2 of the 3 test periods and for whom questionnaire information was available on both parents.

Analytical methods. FEV was analyzed using a linear model. The model included terms for height, age, sex, community of residence, educational attainment of head of household, season of missing FEV, and smoking status of parents. In particular, for child "i" in family "j" the model was

$$FEV_{ij} = B_1 \text{height}_i + B_2 \text{age}_i + B_3 \text{sex}_i + B_4 \text{comm}_j + B_5 \text{educ}_j + B_6 \text{season}_j + B_7 \text{smoke}_j + \epsilon_j + \delta_i$$

where comm_j represented a term (dummy variable) for the residence of the family; smoke_j, a term for the smoking status of each parent; educ_j, a term for educational attainment of the head of household; season_j, a term for possible season of testing missed; ϵ_j represented the variation of FEV from family to family; and δ_i represented the variation of FEV within a family. The dummies were constrained so that the design matrix was nonsingular.

The above model was equivalent to stating that the FEV values could be analyzed using analysis of covariance. Age and height were the covariates, and sex, community, education, season, and parents' smoking habits were the main effects. Because the

design was an unbalanced one, the analysis had to be done using a linear model program. The model as stated required the inversion of a 75 by 75 matrix. Interaction terms were not included because the main effects were relatively small, and the interaction terms would have greatly increased the computational difficulties.

The error sum of squares were split into 2 portions: a between-family variation and a within-family variation. The tests of significance were made using the between-family variation. Because the design was not balanced, these tests were not exact. However, since the majority of families had only one child tested, the tests were approximately correct.

Additional analyses were restricted to those families who answered questions on the presence of a gas stove in the home. Both the effect of maternal smoking and the presence of a gas stove were estimated separately for boys and girls younger than 9 and those between 9 and 13 yr of age.

Results

The results of the initial analysis of the $FEV_{0.75}$ data are shown in table 2. The factors included in the model explain 79% of the total variation, with age and height alone accounting for 73.1% of the variation. The relationship of $FEV_{0.75}$ with both age and height was almost linear over the range of ages and heights observed. The relationships were almost identical to those found by Hamill (29) in his study of vital capacities in children 6 to 11 yr of age. A fairly constant sex difference was observed, with boys showing average values 91 ml larger for the same age

TABLE 2

ANALYSIS OF COVARIANCE FOR CHILDREN WITH BACKGROUND INFORMATION ON BOTH PARENTS

Factor	Degrees of Freedom	Partial Sums of Squares	Mean Square	Approximate F*	Approximate p-value
Age-height-sex adjustments	5	2,019.16	403.8323	19,843.96	< 0.0001
Community	30	22.27	0.9422	25.53	< 0.0001
Education	2	0.05	0.0265	0.72	0.4868
Season missing	3	0.15	0.0509	1.38	0.2500
Parents smoking	35	2.68	0.0765	2.07	< 0.0001
Interaction	25	1.35	0.0542	1.49	0.0520
Fathers	5	.01	0.0014	0.04	0.9991
Mothers	5	1.33	0.2655	7.20	< 0.0001
Packs (mother)	1	1.21	1.2131	32.88	< 0.0001
Other	4	0.12	0.0288	0.78	0.5056
Error (total)	16,613	567.17	0.0341		
Between family	12,748	470.44	0.0369	1.48	< 0.0001
Within family	3,865	97.73	0.0250		

Multiple $R^2 = 0.78978$

Prediction equations:

Boys $FEV_{0.75} = 2.274 + 0.0231$ age (yr) $+ 0.0267$ height (cm.)

Girls $FEV_{0.75} = 2.239 + 0.0248$ age (yr) $+ 0.0261$ height (cm.)

and height. The prediction equations for boys and girls are given in table 2.

Pulmonary function test results have been shown to vary seasonally (30, 31). Therefore, since each child was required to be in the analysis only 2 of the 3 seasons, additional terms were added to adjust for missing seasons. This result was not statistically significant, although children who were tested all 3 seasons tended to have higher FEV values than those who missed a season.

Using educational attainment of head of household and density of people per room alternatively as indexes of socioeconomic status did not affect FEV values. Socioeconomic variation, as measured by these factors, did not appear important.

The variation between families was about 50% greater than the variation within families. This showed clear evidence of familial aggregation. The estimated intraclass correlation was 0.26 ($p < 0.0001$).

Of the remaining factors, differences between the 31 communities accounted for the greatest amount of variation. Ambient air pollutant variables were included in an attempt to explain the sums of squares labeled community variation. No pollutant explained more than 8% of the community variation. Community mean values adjusted for age and height are shown in table 3. Possible explanations for this variation are considered subsequently.

The only other highly significant factor in the analysis was parental smoking, which accounted for 0.1% of the total variation. Each parent was placed in 1 of 6 categories on the basis of the amount he or she smoked. An analysis of ex-smoking parents showed that their offspring's average FEV was virtually identical with the nonsmokers, so the 2 groups were pooled. The 6 remaining categories were based on the amount currently smoked: 0, <0.5 pack, 0.5 to <1 pack, about 1 pack, >1 to 1.5 packs, and 2 packs or more. The 6 categories of smoking for each parent gave 36 possible combinations. The sums of squares for these were split into 3 categories: the amount the mother smoked, the amount the father smoked, and the interaction of the 2. Neither the interaction nor the amount the father smoked were significant at 0.05. The mother's amount, however, was highly significant.

The mothers' amount was split into 2 components: a linear pack function,

and a nonlinear component. The linear pack function explained nearly all of the variation (91%), with an insignificant amount remaining in the nonlinear portion. Thus, parents' smoking could best be represented by the simple function of the amount smoked by the mother. This function was used in further analyses.

The effect of maternal smoking appeared in both sexes and age groups (table 4). The effect on older boys was greater than it was on the children in the other 3 subgroups. The presence of a gas stove in the home had a less dramatic effect (table 4), with the older girls showing a decrease that approached statistical significance ($p = 0.0524$). It is interesting to point out (table 4) that the effect on boys in homes with gas stoves was slightly greater, although not significantly so. The means for the presence of a gas stove were adjusted for community differences so that the comparisons would be within commu-

nities, as was done by Speizer and co-workers (13).

Discussion

Parental smoking. These data indicated a negative association between the amount smoked by the mother and the $FEV_{0.75}$ value of the child living in her home. Similar evidence of a crude dose-response relationship between $FEF_{25-75\%}$ and the number of smokers in a house has been reported by Tager and colleagues (16). Our data revealed only a slight negative and insignificant influence of the amount smoked by the father on the results of his child's pulmonary function test, after considering the amount smoked by the mother. This difference in results might be explained by the method used to gather parental smoking information: the Tager study obtained smoking information by direct interview with each parent, whereas in these data, smoking information was obtained by

TABLE 3

MEAN FEV$_{0.75}$ MEASUREMENTS BY COMMUNITY ADJUSTED FOR AGE AND HEIGHT

Community	Boys 6-9	Boys 9-13	Girls 6-9	Girls 9-13
Charlotte NC				
Sector 2	1.320	1.862	1.252	1.792
Sector 3	1.335	1.874	1.232	1.795
Sector 4	1.368	1.883	1.278	1.826
Birmingham AL				
Inglenook	1.275	1.745	1.147	1.633
Norwood	1.367	1.715	1.108	1.682
Zion City	1.261	1.799	1.158	1.684
Center Point	1.289	1.809	1.190	1.712
Homewood	1.303	1.821	1.217	1.716
Hueytown	1.228	1.781	1.129	1.669
Riverhead NY	1.304	.787	1.168	1.664
Queens NY	1.269	1.744	1.160	1.580
Bronx NY	1.294	1.793	1.194	1.693
Sheepshead Bay NY	1.254	1.768	1.171	1.624
Ridgewood NJ	1.295	1.750	1.191	1.706
Fair Lawn NJ	1.270	1.733	1.140	1.641
Matawan NJ	1.275	1.782	1.162	1.705
Elizabeth NJ	1.229	1.777	1.166	1.712
Ogden UT	1.378	1.921	1.257	1.860
Salt Lake City UT	1.365	1.889	1.252	1.824
Kearns UT	1.319	1.885	1.226	1.752
Magna UT	1.387	1.881	1.224	1.786
Chattanooga TN				
Red Bank	1.201	1.838	1.190	1.740
Brainerd	1.300	1.828	1.170	1.690
Harrison	1.277	1.781	1.188	1.683
Vista CA	1.317	1.858	1.220	1.734
Santa Monica CA	1.358	1.847	1.256	1.802
Anaheim CA	1.325	1.844	1.232	1.748
Glendora CA	1.341	1.865	1.224	1.755
Thousand Oaks CA	1.350	1.838	1.224	1.769
Garden Grove CA	1.317	1.826	1.236	1.756
Covina CA	1.326	1.855	1.224	1.747

TABLE 4

MEAN $FEV_{0.75}$ MEASUREMENTS ADJUSTED FOR AGE AND HEIGHT SUMMARIZED BY COVARIATES

	Boys 6-9	Boys 9-13	Girls 6-9	Girls 9-13
Mother's smoking				
Never or ex	1.315	1.833	1.211	1.734
	(1,933)*	(2,949)	(1,777)	(2,406)
Less than 1 pack	1.301	1.825	1.195	1.729
	(650)	(890)	(597)	(772)
1 or more packs	1.294	1.808	1.195	1.722
	(1,016)	(1,470)	(917)	(1,310)
Gas stove use				
Yes	1.309	1.829	1.203	1.719
	(1,173)	(1,454)	(1,087)	(1,206)
No	1.304	1.825	1.208	1.738
	(1,221)	(2,098)	(1,178)	(1,792)
Education of head of household				
Less than high school	1.296	1.830	1.199	1.739
	(623)	(955)	(531)	(821)
High school	1.308	1.824	1.203	1.728
	(2,121)	(3,040)	(1,926)	(2,593)
More than high school	1.317	1.820	1.209	1.727
	(855)	(1,314)	(834)	(1,076)

* Sample sizes given in parentheses.

a self-administered questionnaire and was reported for both parents by only one parent (usually the mother). It may well be that this method of data collection left us with smoking data that was more accurate for the mothers (self-reported) than for the fathers (reported by another person). Although conjectural, this reasonably could account for the low explanatory power of our father-smoking factor; alternatively, the greater significance of a mother's smoking on the results of her offspring's test may be due to the greater time spent with the child.

Other studies have not found an association between parental smoking and test performance by children. Leeder and associates (15) found no effect on peak expiratory flow rates. This was somewhat inconsistent with our results since our flow rates were strongly correlated with $FEV_{0.75}$ (32, 33), but the investigators tended to attribute this result to small sample size. In Shilling and co-workers (34), although the results suggested a relationship between the amount the mothers smoked and maximal expiratory flow at 50% of FVC among their daughters (if they had never smoked), the investigators concluded parental smoking had no effect on the children's lung function. Finally, Speizer and co-workers (13), working with 8,120 white children between 6 and 10 yr of age, did not find an association between FEV_1 and parental smoking. This finding was possibly due to the age of the subjects? In young children, the FEV_1 may approximate the FVC and be better correlated with lung volume than the $FEV_{0.75}$ used in the present study. We know of no data that support this supposition. The $FEV_{0.75}$ may be more sensitive to variation in airway obstruction, which would suggest that sidestream smoke may have a more obstructive than restrictive effect on the lungs. For a discussion of possible mechanisms, see Tager and colleagues (16).

The Tager results are interesting with regard to the findings of Colley reporting both alone (11, 14) and with Leeder and associates (12) the relationships between the number of smoking parents in a household and the number of respiratory diseases among their children. Other reports, however, are not consistent with the Colley findings. Schilling and co-workers (34) and Lebowitz and colleagues (35) found little or no relationship between smoking parents and the number of reported respiratory symptoms or diseases among their children. They suggested that familial characteristics, such as parent symptoms and family history of respiratory ailments, rather than parental smoking, more readily influence the number of reported respiratory symptoms among children. It is also important to note that within the Tager and colleagues study (16), the investigators did not report a dose-response effect between the number of smoking parents and the number of illnesses in their children.

Gas stoves. Speizer and co-workers (13) using FEV_1 did report a negative association between exposure to a gas cooking stove and the results of a child's pulmonary function test. Our data were less consistent but did show an association that approaches statistical significance of gas stove use and reduced $FEV_{0.75}$ among the sex/age group in which exposures can reasonably be expected to have been highest, e.g., girls 9 to 13 yr of age (table 4). This concentration of effect among females was consistent with the findings of Melia and co-workers (25) who suggested that girls would be more likely to help in the kitchens of their homes—the room with the highest NO_2 exposure in the house (19).

There are 3 possible explanations for these findings. First, older girls may be in the kitchen longer than younger girls. Alternatively, the accumulative length of NO_2 exposure may be more important than simple frequency of exposure. Third, a possible interaction may exist between smoking and NO_2 exposure in older girls. As there was no direct measurement of smoking by children, this last alternative is difficult to assess. In any case, the observed changes were small. However, as set forth by Speizer and co-workers (13), even small differences in age- and height-adjusted lung function in young children may indicate that these children will not develop full lung size in adulthood.

These findings were in contrast to Florey and associates (36) who found that the lung function of 808 school-age children, as measured by $FEV_{0.75}$, peak expiratory flow rate, and mean flow over the mid-half of the FVC, was not related to NO_2 concentrations in their bedrooms or kitchens. It is also important to note that Melia and colleagues (37), although finding respiratory disease and symptom prevalence higher in homes using gas for cooking instead of electricity, concluded that the differences were limited to urban areas and might disappear as the children grew older. Similarly, Keller and co-workers (20) found no differences in reported illnesses, symptoms, or positive findings on physical examination when they compared gas and electric cohorts of school-age children.

Other factors. A significantly greater

amount of the sums of squares attributable to error was found between families than within families (table 2). It was possible, as has been suggested by others (14, 34), that these differences may have been a result of within-family reporting bias. This may be a problem for analyses that consider smoking information, as has been reported by Colley (14). According to Speizer and co-workers (13), however, it is unlikely that within-family reporting bias would be related to the presence of a gas or an electric stove. Our results supported the findings of Speizer and associates (4) and Tager and colleagues (5, 6), which showed that lung diseases tend to aggregate within families.

There were several other potential sources of bias in these data. As mentioned before, the amount the father smoked may be confounded by the reporting method used. It may artifactually have minimized the importance of the father's smoking behavior in our study, whereas it has been found to be significant by other researchers.

Questionnaire information regarding parental smoking and gas stoves could not have influenced technician performance with each child as this information was gathered separately from the pulmonary testing. Regular (daily) calibration of spirometers helped minimize machine biases, but examination for machine bias in some of our sites in other test years revealed that such biasing did occasionally occur. Machine bias, however, was not consistent for any machine in more than a single testing season and, thus, its effect was probably minimal. Bias caused by technician differences should have been countered by the averaging of blows from more than one period. This averaging would have allowed for both a training effect and mixing of technicians period to period. Any remaining technician or machine biases would show up as community differences since different technicians and machines were used in each metropolitan area.

Certain other information would have helped reduce bias and sharpen the distinctions between the exposed and unexposed groups. Unfortunately, children examined in this study were not asked about their personal smoking habits. Confounding could be a problem if the children of smoking parents themselves tended to smoke;

such an association has been reported (38). Possible evidence of this confounding is found in the greater reduction of FEV observed among the older males in our sample, the group that in the early 1970s could be expected to have been smoking most heavily (38). A less likely explanation would be some sort of greater susceptibility of males to side-stream smoke, a susceptibility that would increase with age. Personal smoking is an unlikely explanation for the reduced FEV observed among those 6 to 9 yr of age.

Although no one has assessed the reduction of FEV among smoking children, Tager and colleagues (16) have shown that the maximal $FEF_{25-75\%}$ reduction among smoking children is greater than the $FEF_{25-75\%}$ among children whose parents smoke. Though there are implications from Tager's findings for the interpretation of our results, there are no studies to date assessing the relative impact of children's smoking habits on their FEV versus the effect of the smoking habits of their parents.

In addition to the bias introduced as a result of the linking of the questionnaire and the pulmonary function test data, misclassification of parental smoking is expected to have occurred because of the interval between questionnaire distribution and pulmonary testing. Parents reporting themselves to be nonsmokers may have begun to smoke or vice versa, or the amount of smoking reported may have changed. Furthermore, the amount of present exposure may be less important than the duration of exposure to that amount of side-stream smoke or the total accumulated exposure of a child over his or her youth. None of these questions can be addressed with these data.

Certain points regarding our FEV values should be made. First, to facilitate the testing of a large number of children the digital display of $FEV_{0.75}$ was used. Unfortunately, the digital display of the $FEV_{0.75}$ does not allow for a correction of submaximal effort at the beginning of a test. In a large-scale epidemiologic study, the use of a visual record to evaluate test performance is problematic. The technological advancement of the spirometer since our data collection, however, has alleviated many of the difficulties. Gaensler (39), in discussing procedures for pulmonary function testing in

epidemiology, made a number of detailed recommendations regarding the use of the spirogram (or other record) to evaluate test performance. Second, our recording of only the highest value in each test period favored selection of tests only minimally influenced by submaximal effort. The averaging of values from more than one test period would also allow for a training effect to help minimize this (submaximal) effect. Comparison of these values with $FEV_{0.75}$ readings from machines that allow correction should show the latter values to be somewhat higher. Third, other information, which was not available from these data, such as the variation in all FEV values for each child, the effect on the community, maternal smoking, or gas stove effect by including only children free of respiratory symptoms, the adequacy of the correction for seasonal effect, the amount of mixing of machines and technicians, and the variation found when calibrating the instruments each day, would have helped assess the reliability and validity of the spirometry data.

In summation, the effect of parental smoking on a child's breathing has been observed. The impact of a mother's smoking shows a clear dose-response relationship with a small but significant reduction in her child's ability to exhale air quickly from his or her lungs. The importance of the father's smoking habits is uncertain. The effect of gas stove exposure, which approached statistical significance, was observed in the group most likely to be at risk of highest exposure—older girls.

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Lebowitz, M.D., Armet, D.B., Knudson, R. "The Effect Of Passive Smoking On Pulmonary Function In Children" Environment International 8: 371-373, 1982.

The authors of this study conducted an investigation of ventilatory function in 344 nuclear families in a representative population sample in Tucson, Arizona. Household aggregation of body mass was investigated as a possible confounding factor in the reported association between impaired lung function and parental smoking. The authors report that "when household aggregation of body mass was taken into account, there was no relationship of children's pulmonary function values to parental smoking." The study concludes with the statement that "[i]t must be concluded that passive smoking in the family, usually due to parental smoking habits, does not seriously affect permanent markers of respiratory disease such as pulmonary function."

THE EFFECT OF PASSIVE SMOKING ON PULMONARY FUNCTION IN CHILDREN

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A study of ventilatory function was conducted in 344 nuclear families in a representative community population sample in Tucson, AZ. Household aggregation of pulmonary function, which is dependent on household aggregation of body mass, might affect the relationship of children's pulmonary function to parental smoking. When household aggregation of body mass was taken into account, there was no relationship of children's pulmonary function values to parental smoking. The trend, in the opposite direction, was similar to that found by Speizer *et al.* (1980a), but was not significant in this study. It must be concluded that passive smoking in the family, usually due to parental smoking habits, does not seriously affect permanent markers of respiratory disease such as pulmonary function.

Introduction

There has been some controversy surrounding the issue of whether passive smoking in households effects the respiratory health of children (NRC, 1981). Some investigators have reported that childhood symptom rates appear related to parental smoking, whereas others disagree. However, it is better to utilize pulmonary function to determine this effect, inasmuch as symptom reporting may show tendencies for parental biases (Cederlof and Colley, 1974; Lebowitz and Burrows, 1976; Schilling *et al.*, 1977). One study by Tager *et al.* (1979) showed the effect of parental smoking on FEV_1 utilizing Z scores. A similar analysis from the same laboratory in six other, different populations (Speizer *et al.*, 1980a) showed opposite results. Tager *et al.* (1976) also showed that there was household aggregation of pulmonary function values, which might influence such a relationship. This study has demonstrated the relationship of active smoking to ventilatory impairment (Knudson *et al.*, 1976; Burrows *et al.*, 1977), as has been found by others.

This paper attempts to examine the effects of parental smoking on children's pulmonary flow and volumes after correcting for any familial aggregation of ventilatory function and body size.

Methods

The Tucson Epidemiological Study of Airways Obstructive Diseases, which provided the data base for these analyses, has been described previously (Lebowitz *et al.*, 1975). Briefly, it is a multistage stratified cluster sample of white non-Mexican-Americans in the Tucson area, where stratification was on age of head of household and on social status. Of the 1655 families studied (approximately 3800 individuals), families with children biologically related to the parents were chosen; these represented 344 households and about one-half of the population (1400). In the first year of this study (1972-1973), pulmonary function tests had been satisfactorily completed on over 90% of those age 6 and over using techniques previously described (Knudson *et al.*, 1976). Smoking habits in adults have been described previously (Burrows *et al.*, 1977); they are similar to those found elsewhere and cover the whole range of amount and duration of smoking.

These nuclear families were divided also into parent-child, spouse, and sibling pairs, the former using oldest children, by sex. Z scores [standard normal deviates $Z_i = (x_{ij} - \bar{j})/s_j$, for i individuals and j age-sex groups] were calculated for forced vital capacity (FVC), forced expiratory volume in one second (FEV_1), maximum flow at 50% of the vital capacity (V_{50}), and maximum flow at 75% of the expired vital capacity (V_{75}), within each sex-age group represented in the parent-child pairs. The Z scores were used in analyses of variance to correct for genetic components of body mass in pulmonary function parameters and to detect relationships between parental smoking and children's pulmonary function.

M. D. Lebowitz, D. B. Armet, and R. Knudson

Most houses in this study, as determined by survey, are 1800–2400 ft², not more than 20 years old, have typical 8 ft ceilings, have screened windows, and have central heating and air cooling (usually with filters for both systems). They are kept relatively closed in summer and winter, but are somewhat more open in spring and fall. Air exchange rates have not been measured in this study, but are estimated using published information (NRC, 1981) at between 0.4 and 2.0 per hour, depending on season and use of forced air systems. Indoor pollutant levels were not measured in all of these houses as part of this study. Infiltration of suspended particulate has been measured in about 41 houses (Lebowitz et al., 1982) and is low; though indoor generations is not. Carbon monoxide (CO) indoors and out has been also measured (Lebowitz et al., 1982) and are low as well. The use of types of stoves has been measured in only some families (Lebowitz et al., 1982). Outdoor levels of particulate alone are high in this area, but it is a silica quartz particulate. Nitrogen dioxide and CO are variable, but not in excess of NAAQS (Pima County, 1981).

Results

It was found that there was a household aggregation of pulmonary function values and of body size. Body size is the key determinant of ventilatory function values (Knudson et al., 1976). When the household aggregation of body size was corrected, there was no household aggregation of pulmonary function that was still significant. Therefore, all pulmonary function values were expressed as percent predicted where the children's prediction equations use their own body size values, their age, and the body size values of their parents. Body size values used included height, weight, sitting height, and the ponderal index (H/W 1/3). Parents' pulmonary function values were expressed as percent predicted, where the prediction equations used their body size values and their ages. Z scores were then calculated from these percent-predicted values for the age and sex groups (see above).

Analyses of parent-child, spouse, and sibling pairs by the smoking habits of the family members did not show any significant correlations of passive smoking with pulmonary function. This was true whether children's smoking or not smoking was accounted for, and was also true regardless of whether the parents had airway obstructive disease or abnormal pulmonary function tests. It was also independent of family size. Analyses of variance were performed for the children's pulmonary function test values by smoking in the household, by whether both parents smoked, or whether the mother smoked, father smoked, or neither. The total number of nuclear families was reduced to 271 when both parents and all the children age 6 and over in the household had satisfactory pulmonary function data. As can be seen in Table 1, none of the results were statistically significant. Analysis by amount of parental smoking yielded similar results.

In subsequent years of this study, further symptom information and history was collected. Analysis of these data in relation to passive smoking, using previous methods (Lebowitz and Burrows, 1976), indicated no relation to present or past symptoms, including persistent wheeze or early childhood lower respiratory tract illness. Further analysis awaits collection of more longitudinal ventilatory function measurements on the children.

Discussion

The effects of similar pollutants (specifically NO_2, CO) from the use of gas stoves on children's and adults'

Table 1. Children's pulmonary function by parental smoking in nuclear families.

Parental Smoking		n	FEV, (Z-score)*		FVC (Z-score)	
			Mean	SD**	Mean	SD
Neither smokes		48	−0.121	0.993	−0.082	0.997
Mother smokes		35	−0.157	0.812	−0.157	0.925
Father smokes		92	−0.042	0.970	−0.059	0.913
Both smoke		96	+0.232	1.059	+0.186	1.062
	Total	271	0.026	0.996	0.011	0.988
ANOVA:			$p = 0.0796$		$p = 0.1798$	
			$\dot{V}^{max}_{50\%}$ (Z-score)		$\dot{V}^{max}_{75\%}$ (Z-score)	
Neither smokes		48	−0.160	1.194	−0.075	1.058
Mother smokes		35	−0.147	0.848	+0.004	0.888
Father smokes		92	−0.174	0.945	−0.173	1.011
Both smoke		96	+0.150	0.985	+0.202	0.972
	Total	271	−0.0002	0.998	−0.0001	0.998
ANOVA:			$p = 0.2443$		$p = 0.072$	

*See text for explanation.
**SD = standard deviation.

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symptoms and pulmonary function were explored separately, inasmuch as previous studies indicate such potential effects (Speizer et al., 1980b; Comstock et al., 1981). In a substudy, gas stove use was related to acute symptoms only. Analysis in relation to chronic lung disease and ventilatory function had been performed on the total population of 1655 families; gas stove usage was not related to these measures of disease (Lebowitz, 1977). In that same study, it was shown that ambient outdoor particulate matter was slightly related to those measures of disease, but household size and type of house were not (after controlling for socioeconomic status). Socioeconomic status has little independent contribution to pulmonary function (or disease) once more important factors are considered, such as active smoking (Lebowitz, 1982). Thus, these other factors were not part of the analyses reported herein.

It is possible that correction for family body size concordance is not always necessary (Schilling et al., 1977; Speizer et al., 1980a, 1980b). The presence of persistent symptoms, such as wheeze, may be important in some populations (Weiss et al., 1980), but were not in this population. However, consideration of fuel used for heating and cooking is necessary, especially when passive smoke appears important (Speizer et al., 1980a, 1980b); Comstock et al., 1981; NRC, 1981). Results, especially in lower socioeconomic classes or in developing countries, could be misleading otherwise. On the other hand, there still may be an effect of passive smoking, even when accounting for other exposures, in some circumstances and/or some communities, dependent on environmental circumstances, home ventilation factors, and social class.

A more extensive discussion of these factors and their interactions can be found in the National Research Council report (1981) and in an editorial by Frank and Lebowitz (1981).

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Dodge, R. "The Effects of Indoor Pollution on Arizona Children"
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ABSTRACT. The respiratory health of a large group of Arizona school
children who have been exposed to indoor pollutants-tobacco smoke
and home cooking fumes-is reported. A significant relationship
was found between parental smoking and symptoms of cough, wheeze,
and sputum production. Also, children in homes where gas cooking
fuel was used had higher rates of cough than children in homes
where electricity was used. No differences in pulmonary function
or yearly lung growth rates occurred among subjects grouped by
exposure to tobacco smoke or cooking fuel. Thus, parental smoking
and home cooking fuel affected cross-sectional respiratory symptom
rates in a large group of Arizona school children. Study of
pulmonary function, however, revealed no lung function or lung
growth effects during 4 yr of study.

The Effects of Indoor Pollution

on Arizona Children

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ABSTRACT. The respiratory health of a large group of Arizona school children who have been exposed to indoor pollutants—tobacco smoke and home cooking fumes—is reported. A significant relationship was found between parental smoking and symptoms of cough, wheeze, and sputum production. Also, children in homes where gas cooking fuel was used had higher rates of cough than children in homes where electricity was used. No differences in pulmonary function or yearly lung growth rates occurred among subjects grouped by exposure to tobacco smoke or cooking fuel. Thus, parental smoking and home cooking fuel affected cross-sectional respiratory symptom rates in a large group of Arizona school children. Study of pulmonary function, however, revealed no lung function or lung growth effects during 4 yr of study.

INDOOR AIR POLLUTION has been reported to adversely affect human health. While various occupational lung diseases have long been recognized as secondary to indoor pollution, more recent reports have concluded that the general population is also at risk from exposure to indoor pollution.[1-3,6,8] Among the forms of indoor pollution which may affect humans are tobacco smoke[2] and cooking fumes.[3] Children, because they are usually nonsmokers, have been studied most frequently. Children of smoking parents have been observed to have more respiratory symptoms and lower lung function than children of nonsmokers.[4,5] Similarly, children living in homes where gas is used as the cooking fuel have been reported to have more respiratory problems than other children.[6]

The results of studies of indoor pollution, however, have not been consistent. Some investigators have not found that parental smoking or home cooking fuel are important determinants of childrens' respiratory health.[7,8] At present, these disparate findings are unexplained, but population or methodological differences in studies may be responsible. For example, children living in milder climates may be exposed to lower levels of indoor pollution than children in colder climates. Also, studies to date have been cross-sectional in nature, perhaps producing more variable results than longitudinal studies would.

The author, therefore, chose to conduct a longitudinal study of Arizona children who were exposed to indoor pollutants, findings of which are reported herein.

METHODS AND MATERIALS

The subjects of this study lived in small communities in Arizona: Morenci, San Manuel, and Kingman. Morenci and San Manuel have large copper smelters at the edge of town, but Kingman has no such pollution source. A comparison of respiratory health of the children grouped by exposure to smelter smoke revealed no differences, except in the prevalence of cough.[9] The communities had similar populations (range 4,000 to 7,312) and elevations (range 3,300 to 4,000 ft). The most important demographic difference among the towns was the percent of the subjects who were Mexican-Americans. Only 5% of the Kingman subjects were Mexican-American, whereas 40% of the San Manuel subjects and 57% of Morenci subjects were Mexican-American. Students, and parents of students, in the third or fourth grade in all

schools of Morenci and in one school each in San Manuel and Kingman were contacted. The schools in San Manuel and Kingman were selected because of relatively low out-migration rates. In 1978, 379 students were enrolled at the above-mentioned schools.

In 1979, the students whose parents had declined to participate in 1978, and a new cohort of third graders in the same schools, were contacted. By the end of 1979, 676 students from these schools were participating in the study. The participation rate at the end of 1979 was 76.3%, i.e., 676 of the 884 students contacted in 1978 or 1979 were enrolled. According to the percent of students with Spanish surnames on school enrollment lists, study participation was roughly equal in the two ethnic groups.

Enrolled subjects' parents completed questionnaires on enrollment in 1978 or 1979. The questionnaires contained sections concerning the subjects, their mothers, and their fathers. The majority (62.67%) of the parents completed follow-up questionnaires in 1980.

A few subjects completed the follow-up questionnaire only. The first questionnaire contained questions selected from the questionnaire of the Tucson Epidemiologic Study of Obstructive Lung Disease.[10] The follow-up version contained the same questions plus some new questions about home cooking and migration. Based on the parents' responses to specific questions on either the 1978–79 questionnaire or the follow-up one, prevalence rates for various respiratory problems were established. For example, if the response was YES to the question "Does he or she ever have wheezing or whistling in the chest?" the subject under consideration was listed among those with "wheeze."

Another brief questionnaire was administered to the students who were in the sixth grade in 1980. Questions about cigarette smoking and the symptoms of cough and wheeze were asked. No students reported daily cigarette smoking.

Spirometry was performed on each child with either of two rolling dry-seal CPI spirometers. These two instruments were calibrated before each set of tests and were used all 4 yr with approximately one-half of the children using each one each year. No efforts were made to select which children blew into which machine. A nurse-interviewer with extensive experience in pulmonary function testing and the author conducted the testing. Each child was seated, instructed on performing a maximum expiratory maneuver, and given nose clips. Each child then completed at least three maneuvers. Further efforts were obtained from children who did not produce a second best forced vital capacity (FVC) within 5% of their best FVC. The single best forced expiratory volume in one second ($FEV_{1.0}$) was used in the analyses. These values were corrected for barometric pressure and temperature.

Of the 676 children who participated in the study, and who had the sections of the questionnaires completed about their health, 628 had all additional questions completed which asked about their parents' health (Table 1). The discrepancy primarily reflects the number of single-parent families in which questionnaires for a father were not completed. Also, 419 children's parents completed the 1980 questionnaire, which asked about home cooking fuel (Table 2). Of the 676 subjects, 558 had both a satisfactory pulmonary function test result and questionnaire responses to ques-

Table 1.—Prevalence of Various Respiratory Problems in Subjects Grouped by Parental Smoking

	Parent Reports % with					Child Reports % with		
	N	Asthma	Wheeze	Sputum	Cough	N	Wheeze	Cough
Both parents smoke	146	7.6	41.1†	12.3†	27.4*	28	21.4	14.3
Anglo-whites	116	7.8	42.2	12.1	24.1			
Mexican-American	30	6.7	36.7	13.3	40.0			
Adjusted rate‡	146	7.5	40.0†	12.0†	27.8*			
One parent smokes	185	5.5	28.0†	11.4†	23.2*	34	11.8	5.9
Anglo-whites	102	7.9	32.0	10.8	25.5			
Mexican-American	83	2.5	22.9	12.0	20.5			
Adjusted rate‡	185	5.2	27.9†	10.9†	23.0*			
Neither parent smokes	297	4.1	27.9†	6.7†	14.1*	62	8.1	6.5
Anglo-whites	168	5.4	31.0	6.5	13.7			
Mexican-American	129	2.3	24.0	7.0	14.7			
Adjusted rate‡	297	4.1	27.6†	6.4†	14.6*			

*The rates of cough are significantly different among comparable subjects ranked by parental smoking ($P < .01$ by trend chi square).
†The rates of these symptoms are different among comparable subjects ranked by parental smoking ($P < .05$ by trend chi square).
‡Rate adjusted for differences in rates of parental smokers among areas of study.

tions about parental smoking. The results of the testing of these subjects are displayed in Figure 1. A cohort of 120 8-yr-olds, 163 9-yr-olds, and 87 10-yr-olds produced most of the results. These subjects all had at least three annual tests during the 4 yr of the study. Thus, among the test results displayed by age at testing in Table 1, 120/171, 277/365, 371/443, 307/356, and 192/209 of the tests (82.1%) were produced by the cohort with at least three annual tests. Other results are for subjects who had only one or two annual tests.

Of the 676 subjects, 427 had at least one test result and questionnaire response to home cooking and were included in Figure 2. A cohort of 107 8-yr-olds, 134 9-yr-olds, and 79 10-yr-olds produced most of the results in Figure 2.

In Table 3, only the 472 subjects who had (1) a minimum of two consecutive annual tests and (2) appropriate questionnaire responses to parental smoking and in the lower portion of the Table, the 407 subjects who had (1) a minimum of two consecutive annual tests and (2) appropriate questionnaire responses to home cooking are included. A cohort of 119 8-yr-olds, 162 9-yr-olds, and 87 10-yr-olds produced 89.5% of the data for subjects grouped by parental smoking by undergoing annual testing at least three times. A similar, but slightly smaller cohort produced 92% of the data for the subjects grouped by home cooking.

Chi square, trend chi square, and analysis of variance are the statistical methods used in this report.[11]

RESULTS

Table 1 shows the rates of various respiratory symptoms and asthma in the subjects both overall and when grouped by parental smoking and ethnic background. A significant relation between parental smoking and each of the symptoms of wheeze, sputum production, and cough occurred ($p < .05$ by trend chi square). Because symptoms occurred more frequently in children from certain areas, the rate of symptoms are also shown with adjustment for the slight differences in the rates of parental smoking among the areas where children lived. Again, a significant trend occurred.

In an attempt to avoid the possible bias of smoking parents more readily reporting symptoms in their children than nonsmoking parents, a subset of older subjects were asked about cough and wheeze, the results of which are shown in Table 1. While the differences did not reach statistical significance, children of smoking parents reported more symptoms than children of nonsmoking parents.

Table 2 shows the rates of symptoms and asthma among the subjects grouped by home cooking fuel. The rate of cough was higher ($P < .05$ by chi square) in children who lived in homes where gas was used as a cooking fuel. In the Table, an adjustment for differences in home cooking fuel in the different areas of residence was made, as in the analysis of the effects of parental smoking, with little change in the rates.

The results of pulmonary function testing in the children are in Figures 1 and 2 and Table 3. The figures display $FEV_{1.0}$ vs. age at time of testing. Table 3 shows lung growth in the subjects who had at least two annual testings 1 yr apart. Lung growth was calculated by subtracting
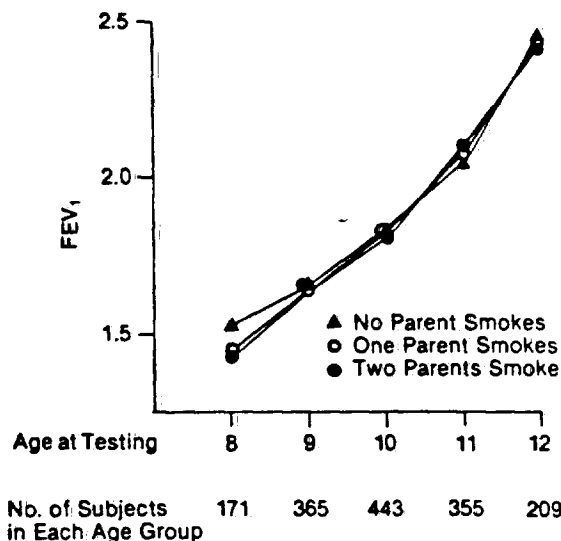
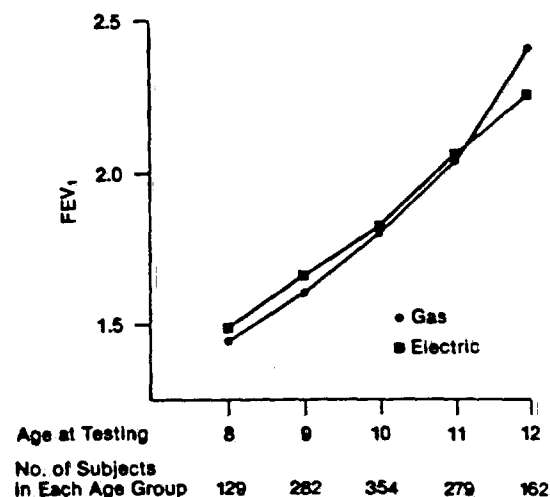Fig. 1. Lung Function in Subjects Grouped by Parental Smoking.

Age at Testing	8	9	10	11	12
No. of Subjects in Each Age Group	171	365	443	355	209

Legend: ▲ No Parent Smokes; ○ One Parent Smokes; ● Two Parents Smoke

Fig. 2. Lung Function of Subjects Grouped by Home Cooking Fuel.

Age at Testing	8	9	10	11	12
No. of Subjects in Each Age Group	129	282	354	279	162

Legend: ● Gas; ■ Electric

$FEV_{1.0}/Height^3$ for 1 yr from $FEV_{1.0}/Height^3$ for the year before. The formula is:

$$Lung\ Growth = FEV_{1.0_{age+1}} / (Height_{age+1})^3 - FEV_{1.0_{age}} / (Height_{age})^3$$

Parental smoking and home cooking fuel did not consistently affect yearly lung function or lung growth.

DISCUSSION

The present report shows that children of smoking parents and children living in homes where gas is the cooking fuel had more respiratory symptoms than other children.

Table 2.—Prevalence of Various Respiratory Problems in Subjects Grouped by Type of Home Cooking Fuel Used

	N	Asthma	Wheeze	Sputum	Cough
Subjects with gas as home cooking fuel	340	4.7	30.6	10.3	20.3*
Adjusted rate†		4.4	31.1	10.1	19.7*
Subjects with electricity as home cooking fuel	79	3.8	29.1	3.8	8.9
Adjusted rate†		3.1	26.7	4.7	10.0

*Rate of cough is significantly higher in subjects with gas home cooking fuel ($P < .05$ by chi square).
†Rate adjusted for differences in rates of gas home cooking fuel among areas of study.

Despite the higher rate of symptoms, however, these subjects had no impaired lung function or lung growth during the 4-yr study. Because of the population studied and the methods used, these result have limited application.

The subjects studied do not represent the general population well. Roughly two-thirds of the children lived in Arizona smelter communities. The author has previously described that the smelter town children, who have been exposed to relatively high levels of sulfur dioxide have a higher prevalence of cough than other children, but comparisons of other symptoms and lung function revealed no differences.[9] Still, smelter town children may be particularly hardy and resistant to the effects of tobacco smoke or gas cooking fumes. When the non-smelter town children were analyzed separately, the results did not differ qualitatively from those when the entire cohort was analyzed. Socioeconomical status differed when the children from different areas were compared, but the status did not affect symptom rates or lung function. Thus, the non-smelter town children and smelter town children appeared to be similarly affected by the variables of parental smoking and home cooking fuel.

The subjects were not randomly selected members of the communities. Approximately one-fourth of the students eligible did not participate, and about 35% of those who did participate contributed only one or two acceptable yearly lung function tests. The subjects who participated for 3-4 yr, then, may not be representative of the general population.

The methods used also limit the application of the study results. No measurements of indoor pollutants were made, therefore, the relation of questionnaire information to actual exposures is unknown. In addition, the questionnaires only asked about parental smoking. While the households with two smoking parents averaged 5.2 persons per household, the same number as households with non-smoking parents, other smokers undetected by the questionnaires may have been present or parents who smoked but did not live with the subject may have been absent. Such persons would have blurred the groupings used in the present analyses.

Despite the above limitations, the study provides evidence that parental smoking and home cooking do not produce serious respiratory problems in Arizona children.

I found, as have others,[4] that children of smoking parents have more respiratory symptoms than other children. To avoid parental reporting bias,[12] all the 1980 sixth graders were asked about respiratory symptoms. While the differences did not reach statistical significance, they again suggested the children of smokers had more symptoms.

Table 3.—Lung Growth of Subjects Expressed as $FEV_{1.0_{age+1}}/(Height_{age+1})^3 - FEV_{1.0_{age}}/(Height_{age})^3$

	N	Age 8-9 yr	N	Age 9-10 yr	N	Age 10-11 yr	N	Age 11-12 yr
Both parents smoke	22	61.84*	62	63.40	73	65.28	47	66.40
One parent smokes	41	68.54	87	65.21	94	64.50	54	68.07
Neither parent smokes	75	64.94	156	65.34	145	64.13	90	67.75
Gas home cooking	94	65.68	204	65.13	211	64.19	132	67.71
Electric home cooking	29	65.80	49	65.31	46	64.93	23	66.16

*The lung growth is significantly different among the subjects 8-9 yr of age ($P < .05$ by ANOVA).

, Also, in agreement with other investigators,[4] I found that children who lived in homes with gas as the cooking fuel coughed more frequently than the other subjects.

The pulmonary function testing showed that neither parental smoking nor gas home cooking fuel adversely affected lung function or yearly lung growth. Tager et al.[5] reported decreased pulmonary function in children of smokers. Others have not found such differences.[7] Similarly, varied results of the effects of gas cooking have been reported.[6,7] To ensure that differences in height did not obscure differences in lung function among the subjects, I also calculated lung growth for each subject who had two or more tests. These results showed that with height cubed taken into consideration, lung growth was not affected by parental smoking or home cooking. Also, when initial lung function was taken into account, by calculating lung growth over the entire period of the study in subjects grouped by initial $FEV_{1.0}$, no differences in the various parental smoking or home cooking groups were found. The results of the present study are good evidence that these

factors do not affect the lung function of children living in the southwestern United States. Indoor monitoring, now in progress, may confirm the suspicion that particulate and nitrogen dioxide levels are much lower in the highly ventilated homes of this region than in colder climates.

In conclusion, while parental smoking and home cooking fuel can influence respiratory symptom rates among Arizona children, these variables do not adversely affect lung function or growth.

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ABSTRACT. In a survey of 1,355 children six to 12 years of age, the risk of hospitalization for respiratory illness among children before age two years was increased when gas was used for cooking at home ($p < 0.001$) or at least one of the parents smoked ($p < 0.02$). The occurrence of cough with colds in children also was significantly increased when one or both parents smoked ($p < 0.001$). Small but signficant increases ($p < .05$) in the mean values of forced expiratory volume at one second, the flow rate at 75 percent of the forced vital capacity, and the forced expiratory flow rate from 25 percent to 75 percent of the vital capacity (FEF25-75) were seen after administering inhaled isoproterenol to children whose parents smoked ($n=89$) but not among children whose parents did not smoke ($n=89$); this was not seen in association with gas cooking. Thus, exposure of children during the first two years of life to gas cooking or cigarette smoking appears to be associated with an increased risk of hospitalization for respiratory illness, and cigarette smoking appears to be associated with a more consistent response to inhaled bronchodilator among six-to 12-year-old children with no other history of chronic respiratory illness.

Relationship of Parental Smoking and Gas Cooking to Respiratory Disease in Children*

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In a survey of 1,355 children six to 12 years of age, the risk of hospitalization for respiratory illness among children before age two years was increased when gas was used for cooking at home (p <0.001) or at least one of the parents smoked (p <0.02). The occurrence of cough with colds in children also was significantly increased when one or both parents smoked (p <0.001). Small but significant increases (p <.05) in the mean values of forced expiratory volume at one second, the flow rate at 75 percent of the forced vital capacity, and the forced expiratory flow rate from 25 percent to 75 percent of the vital capacity (FEF25-75) were seen after administering inhaled isoproterenol to children whose parents smoked (n = 94) but not among children whose parents did not smoke (n = 89); this was not seen in association with gas cooking. Thus, exposure of children during the first two years of life to gas cooking or cigarette smoking appears to be associated with an increased risk of hospitalization for respiratory illness, and cigarette smoking appears to be associated with a more consistent response to inhaled bronchodilator among six- to 12-year-old children with no other history of chronic respiratory illness.

Parental smoking has been shown to be related to increased risk of respiratory illness in children during the first year of life,[1] and to an increased risk of morning cough, respiratory infections, and breathlessness among older children.[2] Specifically, an increased incidence of pneumonia and bronchitis with consequent hospitalizations has been reported among infants whose parents smoked compared to children whose parents did not smoke.[3] Parental smoking also

has been reported to increase the risk of persistent wheeze[4] and symptomatic asthma.[5] In a study of British secondary schoolchildren that showed early morning cough to be more commonly reported by children who smoked, the effect on these smoking children of parental smoking appeared to be additive.[6] A decrease in pulmonary function measurements also has been noted in nonsmoking children whose parents smoked.[7,8]

An association has been similarly shown between respiratory illness in children and gas cooking, apparently from increased levels of nitrogen dioxide and nitric oxide in the homes with gas stoves.[9] In addition, pulmonary function measurements performed in school age children were found to be lower in association with the use of gas stoves in the home.[8,9]

The current study was designed to further examine the relationship of parental smoking and gas cooking on the occurrence of respiratory illness and symptoms in children from a midwestern university community. Additionally, we examined the relationship between these environmental exposures and pulmonary functions.

METHODS

Subjects

Children, ages 6 to 12, who attended primary school in the Iowa City School District were contacted after permission was obtained from school administrators. The school district serves a university community. The children were therefore generally from middle and upper social classes. Participating schools included approximately 87 percent of the 2,062 children six to 12 years of age enrolled in the school district. Children from the participating schools were sent home with a letter explaining to parents the purpose of the studies, the information we were interested in collecting and why. The parents were requested to complete a modification of the questionnaire developed by the American Thoracic Society (ATS) for the Division of Lung Disease (DLD) of the National Heart, Lung, and Blood Institute (the ATS-DLD questionnaire)[10] and to return it to us in a stamped, self-addressed envelope. (A copy of the modified questionnaire is available on request from the authors.) Two weeks following the initial distribution of the questionnaires to the parents, another letter was sent as a reminder to parents who had failed to return a completed questionnaire.

In order to determine if nonrespondent parents and their children differed significantly in certain characteristics from those parents who had completed the questionnaires about their children, 200 nonrespondent parents were randomly selected and contacted by telephone by a trained research assistant four weeks after the questionnaires were initially sent to the parents. The parents were each read the part of the questionnaire that related most directly to cigarette smoking and respiratory illness. To ensure that the questions were answered accurately, these pertinent questions from the questionnaire were read aloud exactly as printed and without any elaboration by the research assistant.

Pulmonary Function Measurements

Pulmonary function measurements were obtained from 59 chil-

dren (47 girls and 41 boys) whose parents did not smoke and 94 children (52 girls and 42 boys) whose parents smoked. These children were randomly selected using tables of random numbers from the children for whom complete information was obtained using the questionnaire. All parents were requested to indicate their consent for pulmonary function studies to be obtained from their children, after we had provided a full written explanation of the reasons for obtaining the measurements and the procedures the child would follow during pulmonary function testing. Consent was obtained from 411 (85.6 percent) of the 484 children whose parents did not smoke and 596 (91.1 percent) of the 654 children whose parents smoked. When parental smoking was kept constant, the proportions of children who had cough with cold, cough apart from colds, or phlegm with or apart from colds were not significantly different for consenting parents compared to nonconsenting parents. We therefore felt that our sampling procedure produced a representative population of children.

Children were excluded if there was a history of recurrent respiratory illness or if there was any history of upper or lower respiratory infection during the prior six months. Spirometry was measured with a Jones Pulmonor waterless respirometer. Calculations of the parameters measured were done by the Jones Datamatic Computer with daily calibration. Lung volumes were measured by use of a plethysmograph (model 2000B Cardiopulmonary Instruments) using a 3 L/second Fleisch temperature-controlled pneumotach, with a flow accuracy of ± 1 percent of full scale.

Each child was instructed in the measurement maneuver and was in an upright sitting position. Each test was repeated three to five times, and the best effort was taken. Flow rates and lung volumes were measured before and five minutes subsequent to 1.25 mg inhaled isoproterenol diluted with 2 ml normal saline solution and administered by an open nebulizer.

Analysis of Data

Discrete multivariate analysis was used to study the interactions among factors.[20] In this analysis, maternal and paternal smoking and gas cooking were treated as independent factors, while the frequencies of various respiratory symptoms or illness were the dependent variables. The reported prevalence of respiratory symptoms or illnesses were stratified by parental smoking (mother alone, father alone, both parents, either or both parents, neither parent smokes) and by cooking fuel use. Odds ratio was calculated for each interaction effect. Odds ratios greater than one indicated that the variable had a higher risk for the children and conversely odds ratios of less than one indicated lower risk. A chi-square analysis was used to examine the significance of the odds ratio.

Regression lines were fitted to each of the pulmonary function measurements using the Statistical Analysis System (SAS) using the stepwise procedure.[21] The variables entered in the equation were age in years, sex, weight (kg), and standing height (cm). Lines were fitted separately for children from smoking and nonsmoking environments, as well as for values obtained by pooling these two groups. F-tests were performed as described by Neter and Wasserman[22] to compare the fit of the lines obtained for values for children from the two environments and for the pooled data. Paired t-tests were used to compare the prebronchodilator and postbronchodilator pulmonary functions.

RESULTS

Completed questionnaires were obtained for 1,355 children, or 65.7 percent of the children six to 12 years of age in the school district. Of the 1,355 completed questionnaires, data on parental smoking history was complete for 1,138 (84 percent) of the children. In the remaining 217 questionnaires, either maternal or paternal or both smoking histories were unrecorded or incompletely recorded. The proportion of children with incomplete or no parental smoking history who had cough with or apart from colds, congestion or bringing up phlegm, or had chronic lung diseases was not statistically significantly different from the proportion of children with parental smoking histories who had these symptoms. These questionnaires were eliminated in subsequent analysis. Forty-nine percent of these children were males, and 51 percent were females. Five percent of the children had established diagnoses of chronic respiratory diseases. Two had cystic fibrosis, one had pulmonary tuberculosis, two had diagnoses of chronic bronchitis, and 49 had asthma. When we compared the 200 randomly selected nonrespondent families to our study population, we found no statistically significant differences in the proportion of parents who smoked at home. The proportions of children who had cough with colds, cough apart from colds, or who had congestion or bringing up phlegm with or apart from colds were not significantly different among the two groups.

Fifteen percent of the parents completing the questionnaire indicated they had bronchitis, emphysema, asthma, or other chronic respiratory condition. We found no relationship between the report of chronic respiratory illnesses in parents and the reported prevalence in children of symptoms of cough with colds,

Table 1—*Proportion of Children with Cough with Colds or Hospitalized for Chest Problems Before Age 2 Years, by History of Parental Smoking and Home Cooking Fuel Used*

Home Cooking Fuel	Parental Smoking History (Yes = Parent Smokes)		Percentage of Children Affected (Total Number of Children in the Group)	
	Father	Mother	Cough With Colds	Hospitalization For Chest Illnesses
Gas	No	No	32.8 (137)	5.1 (138)
Gas	No	Yes	35.7 (28)	7.1 (28)
Gas	Yes	No	35.6 (101)	8.0 (100)
Gas	Yes	Yes	30.6 (111)	9.8 (112)
Electricity	No	No	28.9 (83)	2.1 (34)
Electricity	No	Yes	37.7 (69)	8.8 (65)
Electricity	Yes	No	37.7 (69)	5.6 (175)
Electricity	Yes	Yes	44.5 (173)	1.2 (172)

Table 2—Association of Parental Smoking and Gas Cooking with Hospitalization of Children Before Age 2 Years for Respiratory Illnesses

Independent Variables	No. of Children Hospitalized for Chest Illnesses		Odds Ratio	SE	p-Value
	Yes	No			
Fuel used for home cooking					
Gas	28	350	2.4	0.684	0.001
Electricity	25	736	1.0	...	...
Parental smoking					
Father alone smokes	18	260	2.3	0.856	0.022
Mother alone smokes	8	90	2.9	1.279	0.026
Father and mother smoke	13	271	1.6	0.856	0.21
Either or both parents smoke	39	621	2.1	0.666	0.017
Neither parent smokes	14	465	1.0	...	...

cough apart from cold, or bringing of phlegm with or apart from colds. Of the 1,138 children, 31 percent lived in homes where gas was used for cooking, and 69 percent lived in homes where electricity was used for cooking. There was a significant association between parental smoking and the use of gas for cooking. Fathers smoked in 224 (56.4 percent) of the 397 homes where gas was used for cooking, compared to 366 (46.6 percent) of the 786 homes in which electricity was used for cooking ($x^2 = 10.28$, $p < 0.001$). Similarly, mothers smoked in 180 (40.8 percent) of the 441 homes in which gas was used for cooking, compared to 292 (33.7 percent) of the 866 homes in which electricity was used for cooking ($x^2 = 6.33$, $p < 0.05$). The proportion of children with chronic respiratory symptoms by parental smoking and use of cooking fuel are shown in Table 1.

The use of gas for cooking was associated with an increased risk of hospitalization of the children before age two years because of chest colds and other respiratory illnesses (odds ratio = 2.4) independent of parental smoking (Table 2). Any parental smoking also increased the odds ratio. When both parents smoked in a household in which gas was used for cooking, the odds ratio was 2.9 (p=0.0006). Use of gas for cooking was not associated with increased risk of occurrence of cough with colds in the children. How-

ever, parental smoking increased the risk of occurrence of these symptoms (Table 3). Other than the possibility of wheezing and whistling sounds in the chest with colds, none of the dependent variables in Table 4 was significantly associated with parental smoking and/or use of gas for cooking. Also, the frequency of occurrence of ear infections in the children between ages 0 to two years, or two to five years, or the occurrence of wheezing with exercise was not found to be associated with parental smoking or use of gas for cooking.

The mean standing height of 144.2 cm and weight of 37.8 kg for children whose parents smoked was not significantly different from the mean standing height of 145.6 cm and weight of 38.7 kg for children whose parents did not smoke. Mean values for initial measurements of pulmonary function before the inhaled isoproterenol did not differ significantly between children from smoking and non-smoking families. Significant differences in mean values were not seen after bronchodilator inhalation in the children from non-smoking families, but were apparent among children from smoking families for the measurements of FEF75, FEV₁, and FEF25-75 (Table 5). The mean values of the measurements of lung volumes for the two groups of children were not statistically different. Because 28 t-tests were performed for these analyses, adjustment was made by accepting only t-tests with p

Table 3—Association of Parental Smoking and Gas Cooking with Occurrence of Cough with Colds in Children

Independent Variables	No. of Children with Symptoms of Coughs with Colds		Odds Ratio	SE	p-Value
	Yes	No			
Fuel used for home cooking					
Gas	125	252	0.9	0.123	0.55
Electricity	266	495	1.0	...	...
Parental smoking					
Father alone smokes	100	177	1.4	0.228	0.023
Mother alone smokes	36	61	1.5	0.338	0.084
Father and mother smoke	111	173	1.6	0.255	0.002
Either or both parents smoke	247	411	1.5	0.194	0.001
Neither parent smokes	144	366	1.0	...	...

Table 4—Relationship of Parental Smoking and Cooking Gas with Occurrence of Respiratory Symptoms in Children

Independent Variable	No. of Children with Respiratory Symptoms		Odds Ratio	SE	p-Value
	Yes	No			
1. Chest congestion and phlegm with colds					
Gas	70	307	1.1	0.188	0.41
Electricity	126	633	1.0	...	...
Father alone smokes	46	230	1.0	0.213	0.82
Mother alone smokes	19	78	1.3	0.363	0.40
Father and mother smoke	54	229	1.2	0.383	0.28
Either or both parents smoke	119	537	1.2	0.186	0.35
Neither parent smokes	77	403	1.0	...	...
2. Chest congestion and phlegm apart from cold					
Gas	17	345	1.0	0.302	0.99
Electricity	35	708	1.0	...	...
Father alone smokes	12	258	0.9	0.345	0.86
Mother alone smokes	7	87	1.6	0.730	0.30
Father and mother smoke	11	264	0.8	0.317	0.64
Either or both parents smoke	30	609	1.0	0.286	0.98
Neither parent smokes	22	444	1.0	...	...
3. Wheezing and whistling sounds in chests with colds					
Gas	104	273	1.0	0.154	0.56
Electricity	198	561	1.0	...	...
Father alone smokes	74	202	1.2	0.210	0.27
Mother alone smokes	30	67	1.5	0.362	0.12
Father and mother smoke	86	198	1.4	0.241	0.03
Either or both parents smoke	190	467	1.3	0.165	0.03
Neither parent smokes	112	370	1.0	...	...
4. Wheezing and whistling sound in chest apart from colds					
Gas	29	326	0.9	0.222	0.80
Electricity	61	647	0.1	...	...
Father alone smokes	24	235	1.2	0.329	0.52
Mother alone smokes	14	73	2.2	0.761	0.02
Father and mother smoke	16	244	0.6	0.239	0.39
Either or both parents smoke	54	552	1.1	0.257	0.55
Neither parent smokes	36	421	1.0	...	...
5. Attacks of wheezing with shortness of breath					
Gas	30	346	0.7	0.158	0.12
Electricity	83	679	1.0	...	...
Father alone smokes	26	251	0.8	0.211	0.48
Mother alone smokes	12	85	1.1	0.389	0.70
Father and mother smoke	22	261	0.7	0.181	0.14
Either or both parents smoke	60	597	0.8	0.161	0.29
Neither parent smokes	53	425	1.0	...	...

values of <0.002 as significantly different at a 0.05 confidence level (0.05 ÷ 28 = 0.002) The mean percentage changes in the pulmonary function measurements (calculated as the differences between the postvalue and prevalue divided by the prevalues for each patient), however, did not differ significantly between the two groups of children (using an unpaired t-test).

Discussion

Respiratory symptoms and illnesses occur frequently, particularly in the temperate regions of the worlds in preschool and school-age children. Only recently has it been appreciated that parental smoking at home may be associated with an increased risk of occurrence of respiratory symptoms in children. A higher rate of hospitalization of the children before age two years for chest illnesses (bronchitis, pneumonia, etc) was associated with both parental smoking and gas cooking. A significant increase in pulmonary function after an inhaled bronchodilator among children of

Table 5—Flow Rates of Children Before and After Inhaled Isoproterenol

	Children of Smoking Parents			Children of Nonsmoking Parents		
	Mean (SE) Measurements of Flow Rates and Lung Volumes			Mean (SE) Measurements of Flow Rates and Lung Volumes		
Variables	Preisoproterenol	Postisoproterenol	p*	Preisoproterenol	Postisoproterenol	p*
PEFR	5.11 (0.13)	4.97 (0.13)	0.11	5.10 (0.13)	5.05 (0.12)	0.42
FEF25	4.18 (0.12)	4.15 (0.12)	0.71	4.34 (0.11)	4.23 (0.1)	0.11
FEF50	3.22 (0.09)	3.35 (0.09)	0.02	3.25 (0.09)	3.36 (0.09)	0.07
FEF75	1.52 (0.05)	1.76 (0.07)	0.0001†	1.56 (0.06)	1.69 (0.07)	0.11
FEV$_1$	2.23 (0.05)	2.27 (0.05)	0.0002†	2.21 (0.05)	2.23 (0.06)	0.34
FEV$_3$	2.52 (0.06)	2.52 (0.06)	0.48	2.47 (0.06)	2.50 (0.07)	0.17
FEF25-75	2.60 (0.08)	2.82 (0.08)	0.0001†	2.60 (0.07)	2.78 (0.09)	0.03
FVC	2.55 (0.06)	2.57 (0.06)	0.18	2.51 (0.07)	2.53 (0.07)	0.13

*Paired t-test comparing initial pulmonary function measurements and postbronchodilator values.
†Significant at 0.05 level after adjusting for the performance of 28 t-tests.

smoking parents is an interesting additional observation perhaps consistent with previous reports of increased bronchial reactivity in cigarette smokers with normal lung function" and an association between symptomatic asthma in children and parental smoking."

Parental smoking may be associated with different types of respiratory illnesses in infancy compared to the school age. Fergusson et al found an increased risk of infantile lower respiratory illnesses in the last eight months of the first year of the infant's life to be associated with maternal but not paternal smoking. Similarly, Colley et al found that infantile pneumonia was more common when both parents smoked than when neither parent smoked. The risk was intermediate when only one parent smoked. These results are consistent with our findings that hospitalization of children in the first two years of life for bronchitis and pneumonia was associated with parental smoking. However, Fergusson et al did not study the association of parental smoking and use of gas for cooking on respiratory infection rates. Their study is different from ours also, in that they studied respiratory infection rate between four and 12 months of life. Their study was prospective-retrospective in design, and therefore, parental recall may have been more reliable than in our study. In the first year of life, an infant is likely to spend proportionately more time with the mother than the father. Thus, the age of the child at the time of the administration of the respiratory questionnaire may have been an important factor in the finding that maternal but not paternal smoking was associated with respiratory illness in the child.

Weiss et al reported a dose response between prevalence rate of symptoms of persistent wheezing, cough, and phlegm in children and parental smoking. The rate of occurrence of symptoms in children was highest when both parents smoked, intermediate when either parent smoked, and lowest when no parent smoked. However, the authors also found a strong association between the occurrence rate of these symptoms in the children and the prevalence rate for such symptoms in the parents. We found a significant association between parental smoking and the prevalence of cough with colds in the children. However, we did not find any association between parental smoking or the use of gas cooking and the reported incidence of cough apart from colds and chest congestion and bringing up phlegm with or apart from colds. In a study of children whose ages were similar to the children in our population, however, Colley found an association between parental smoking and the occurrence of cough during the day or at night in winter in the children. He also found an association between parental smoking and bringing up "any phlegm from the chest first thing in the morning in winter" by the children. The lack of association between these variables and parental smoking in our study may be attributable to the phrasing of the questions in the ATS-DLD questionnaire, where "in the morning" was not specifically mentioned, and where phlegm production was sought in association with chest colds rather than "in winter." Slight changes in the phrasing of questions can result in substantial differences in the type of responses one obtains."

Flory et al showed an association between the levels of NO$_2$ in kitchens and bedrooms of the homes, and the prevalence of respiratory illness in primary school-children. This association was independent of the children's age, sex, social class, and the number of cigarettes smoked at home. In another study, children six to 11 years old from households with gas stoves had a history of more frequent respiratory illnesses before age two years compared to children from homes where gas was not used for cooking." In a study of schoolchildren in England and Scotland, a reported incidence of coughs, colds going to the chest, and bronchitis in children from homes using gas for cooking

was significantly higher than for children from homes where electricity was used.[10] Melia et al[11.21] demonstrated that the association between respiratory illness and gas cooking tended to disappear as the children grew older.

The nature of the association of respiratory symptoms in children and gas cooking in the home is yet unclear. Two oxides of nitrogen, nitric oxide (NO) and nitrogen dioxide (NO$_2$), are produced in varying concentrations in homes with gas stoves.[12.13] It has been observed that acute exposure of man and animals to high levels of nitrogen dioxide (NO$_2$) can cause pulmonary edema and death.[13]

A significant reduction in FEF25-75 values was observed in children who smoked, as well as in children whose parents smoked but who were non-smokers themselves.[9] At least one group of investigators has found no association between parental smoking and lung function measurements of the children.[17] In these studies, the children did not receive an inhaled bronchodilator drug. Inhaled bronchodilator medication was administered to children in our study, and we observed statistically significant differences in the mean values of FEF75, FEV$_1$, and FEF25-75 for children whose parents smoked compared to those whose parents did not smoke. The clinical importance of such observed differences in the absolute values of pulmonary function measurements is, however, unclear.

In a recent study of children six to 11 years old from households with gas stoves, small but significant differences were found in FEV$_1$ and FVC corrected for height, compared to children from homes where gas was not used for cooking.[11] These families tended to be poorer and were in the lower socioeconomic class. Florey et al[5] found no significant relationship between lung function measurements and concentrations of NO$_2$ in either kitchen or bedroom. Lung function measurements of peak expiratory flow rates (PEFR) and FEF25-75 for children from homes with gas stoves were not significantly higher than measurements for children from homes with electric stoves. Hasselblad et al,[12] however, found pulmonary function suggestively decreased among nine- to 13-year-old girls in homes with gas stoves and not among younger children.

Based on the findings of this report and from previously published findings, one is led to conclude that parental smoking is associated with a risk of certain respiratory illnesses and symptoms among children living in the same environment. An independent but similar effect is suggested for gas cooking. Children from homes where parents smoke had increased reactivity of airways after bronchodilator therapy, but it is not known if these changes persist or have clinical consequences.

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Myocardial Protection via the Coronary Sinus

The First International Symposium on Myocardial Protection via the Coronary Sinus will be held at the Hotel InterContinental Vienna, Vienna, Austria, February 27-29, 1984. For information, contact the Secretariat, c/o Interconvention, PO Box 80, A-1107 Vienna, Austria.

Diagnostic Imaging

The Department of Radiology, Duke University Medical Center, will present this five-day postgraduate course at the Hyatt Regency Cancun Hotel, Cancun, Mexico, February 12-17, 1984. For information, contact Donald R. Kirks, M.D., Department of Radiology, Duke University Medical Center, Box 3834, Durham, North Carolina 27710 (919:681-2711, ext 286 or 287).

Parental Smoking and Gas Cooking in Respiratory Disease of Children (Ekwo et al)

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LONGITUDINAL STUDY OF THE EFFECTS OF MATERNAL SMOKING ON PULMONARY FUNCTION IN CHILDREN

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Abstract   We investigated the effects of maternal cigarette smoking on pulmonary function in a cohort of children and adolescents observed prospectively for seven years. A multivariate analysis revealed that after correction for previous forced expiratory volume in one second (FEV_1), age, height, change in height, and cigarette smoking in the child or adolescent, maternal cigarette smoking significantly lowered the expected average annual increase in FEV_1 ($P = 0.015$). On the basis of this analysis, it is estimated that if two children have the same initial FEV_1, age, height, increase in height, and personal cigarette-smoking history, but the mother of one has smoked throughout the child's life whereas the mother of the other has not, the difference in the change in FEV_1 over time in the exposed child, as compared with that in the unexposed child, will be approximately 28, 51, and 101 ml after one, two, and five years, respectively, or a reduction of 10.7, 9.5, and 7.0 per cent, respectively, in the expected increase. These results suggest that passive exposure to maternal cigarette smoke may have important effects on the development of pulmonary function in children. (N Engl J Med 1983; 309:699-703.)

PREVIOUS studies have suggested[1-6] that maternal cigarette smoking influences the level of lung function in children. Most of these studies[1-4] used analyses of cross-sectional data that left unanswered questions concerning the quantitative influence of maternal smoking on the development of lung function in children over time. As part of an ongoing study of childhood risk factors for the development of chronic obstructive airways disease, we investigated the effects of maternal cigarette smoking on pulmonary function in a cohort of children observed prospectively for seven years in East Boston, Mass.

METHODS

Selection and Screening of Sample

A 34 per cent random sample was selected from all children five to nine years of age who were enrolled in the public and parochial schools of East Boston, Mass., in September 1974. Between January and June 1975, using materials provided by the Division of Lung Diseases, National Heart, Lung, and Blood Institute interviewers visited the households of the index children and enumerated all residents. The residents of these households, plus the index children, constituted the initial study population. Initial examination of the subjects was conducted in a special neighborhood clinic between January and June 1975. Index subjects were visited in their homes during the school year (September to June), for six annual follow-up examinations; other family members were visited in their homes only for follow-up examinations 3 through 6. Follow-up interviews were conducted, whenever possible, within four calendar weeks of the date of the previous year's interview, usually between 2:00 p.m. and 8:00 p.m. For the initial and first two follow-up examinations, two interviewers were employed. All subsequent examinations were performed by only one of the two original interviewers.

Standardized questionnaires were used to obtain a history of respiratory symptoms and illnesses, as well as a smoking history and demographic data. At the initial examination and first two follow-up examinations, separate questionnaires were used for subjects under 10 years of age and for subjects 10 years or older. A common questionnaire was used for all subjects in the third through sixth follow-up examinations. The questions relating to chronic respiratory symptoms were proposed for lung-program epidemiology studies by the Division of Lung Diseases, National Heart, Lung, and Blood Institute.[7] For children aged 10 or younger, the parents answered all questions except those pertaining to the child's own smoking history; all other children answered all questions themselves. A smoking history was obtained directly from all children during pulmonary-function testing — a time when parents were not present.

Pulmonary-Function Testing

Forced vital capacity was measured while the subjects were in the sitting position, without nose clips, using an 8-liter water-filled, portable, recording spirometer (Survey Spirometer, Warren Collins, Braintree, Mass.), which was calibrated according to a regular schedule. Subjects were encouraged to perform the test until five acceptable tracings had been obtained or until it became evident that they could not perform it adequately. For children in the preteen years, pulmonary-function tracings were considered acceptable if they were at least four seconds in duration (all other subjects were encouraged to blow for at least six seconds) and if the interviewer thought that a maximum effort had been made.

One-second forced expiratory volume (FEV_1) and forced expiratory flow between the 25th and 75th per cent of forced vital capacity (FEF_{25-75}) were measured by standard techniques.[8] When mean values were used, they were calculated as the mean of the best three of five tracings, as recommended by the Division of Lung Diseases, National Heart, Lung, and Blood Institute.[7] All pulmonary-function measurements were corrected to body temperature and pressure saturated with water vapor. Each subject's standing height without shoes was measured to the nearest 1.5 cm. Mean function values were converted into per cent predicted values with the nomograms of Dickman et al.[9] for subjects less than 25 and with those of Ferris et al.[10] for subjects 25 or older.

Definitions of Cigarette Smoking

At any given examination, subjects who were 20 or older were defined as never having smoked if they had never smoked or had smoked no more than one cigarette per day for more than one year or no more than 20 packs during their lifetime. "Current smokers" were defined as those who had smoked more than these amounts and who had been smoking within one month before the time of interview, for the initial examination, or for the entire year before and including the time of the interview, for the follow-up examinations. Exsmokers were defined as those who had stopped smoking more than one month before the interview. Subjects 19 or younger were considered never to have smoked if they had never smoked or

had smoked no more than one cigarette per week, as reported at each examination; otherwise, they were identified as "ever smokers" for that examination.

Methods of Data Analysis

Per cent predicted values for FEV_1 and FEF_{25-75} for subjects 19 years or younger were divided into sex-specific five-year age groups (5 to 9, 10 to 14, and 15 to 19); per cent predicted values for subjects age 20 or older were divided into two sex-specific groups. Within each group, subjects were ranked, and the ranks were then converted to a cumulative frequency distribution. Each rank was then assigned a Z score from a table of areas under a standard normal curve. [11] Each score corresponds to the position of the subject's per cent predicted value in the cumulative frequency distribution; the mean score in each group was 0, with a variance of 1.

The mean Z score (FEV_1, FEF_{25-75}) for the first six years was calculated for each child as the average of all yearly values over this period. Because a variable number of annual observations was available for each child, the children were stratified according to the number of observations that were available to calculate their six-year mean values. (The median number of measurements was three, and the range was one to six. Sixty-two subjects, or 10.2 per cent, had six measurements; only index subjects five to nine years of age at intake could have had as many as six. Forty per cent of the subjects had four or more.) The six-year mean Z scores for FEV_1 and FEF_{25-75} were rank-ordered separately within each stratum. For each lung-function measurement, the ranks were grouped into the lowest 20 per cent, the middle 60 per cent, and the highest 20 per cent of the ordered values. These groupings were then combined for all the strata. This procedure permits comparisons of mean values in children who had different numbers of examinations.

To estimate the effect of parental smoking after controlling for the effects of the child's age, sex, initial height, increase in height, and personal smoking status, we used a Markov-type autoregressive model (Rosner B, et al.: unpublished data) similar to that proposed by Korn and Whittemore [12] for a dichotomous outcome. Chi-square analyses were performed with programs designed for programmable calculators by Rothman and Boice. [13]

RESULTS

The study group consisted of 1156 white children from 404 families. At each examination, acceptable measurements of FEV_1 were obtained in more than 70 per cent of the available children (Table 1). The children in whom measurements of lung function were obtained were significantly more likely to be younger and female than those in whom such measurements were not obtained (Table 1). However, the children were comparable with regard to chronic respiratory symptoms, mothers' education, mothers' smoking history, and type of home heating. In 75 per cent of the children in whom acceptable measurements of lung function were obtained in any given year, two or more such measurements were obtained over the first six examinations.

The percentage of children with mothers who were current smokers, as ascertained at either the initial or sixth examination, was highest among children with the lowest average levels of FEV_1 over the first six examinations (Fig. 1). The trend toward decreasing frequency of maternal smoking with increasing mean level of FEV_1 over the six examinations was significant (χ^2, trend = 11.1, P<0.001). Analysis of the FEF_{25-75} levels gave results virtually identical to those for FEV_1. Similarly, analyses restricted to children who were cumulative "never smokers" at the sixth examination and to those with more than two pulmonary-function examinations gave results that were identical to those shown in Figure 1. No uniform trends were observed in comparisons of the smoking habits of fathers and the mean level of FEV_1 or FEF_{25-75} over the first six examinations.

The results of the autoregressive model relating change in FEV_1 over a one-year period to the mother's and the child's smoking status, after correcting for previous FEV_1, age, height, and one-year growth in height, are given in Table 2. The analysis, which is based on data from all seven examinations, shows that the offspring of mothers who were current cigarette smokers had significantly reduced annual increases in FEV_1 after correcting for all the other variables in the table (P = 0.015). The total of the variance in FEV_1 at any point in time explained by the model was 92.5 per cent.

The effects of the mother's and the child's smoking habits on the change in FEV_1 in the child appeared to be additive, since no significant interaction was detected between these effects. Furthermore, neither the main effect of the father's smoking status nor the interaction of the father's and mother's smoking habits contributed significantly to the prediction of change in FEV_1 in the child.

The projected effects of the mother's smoking status on the annual rate of change of FEV_1 in a male child,

Table 1. Median Age and Age Range of Study Population, According to Sex, Number of Examinations, and Presence or Absence of Lung-Function Measurements.*

Examination Number†	Lung-Function Measurement		Total No.‡	No Lung-Function Measurement		Total No.‡
	Male	Female		Male	Female	
	median age; range	median age; range		median age; range	median age; range	
1	8 (443); 4-25	8 (409); 4-23	852	7 (169); 4-23	6 (135); 4-20	304
4	11 (381); 6-26	11 (336); 6-24	717	14 (60); 6-28	14 (31); 6-27	91
5	12 (345); 7-27	12 (313); 7-28	658	15 (91); 8-24	15 (39); 9-21	130
6	12 (332); 7-28	12 (301); 6-24	633	15 (106); 7-26	15 (72); 7-26	178

*Figures in parentheses are numbers of children.

†The results of examinations 2 and 3 are not shown, since only children aged 5 to 9 years in the solution of the cohort were studied. At examinations 1 and 2, respectively, 83.4 per cent and 86.9 per cent of available children had lung-function measurements.

‡Not all of the children observed after the first examination had been seen at the previous examinations; since subjects who were missed at any preceding visit were studied whenever they were available.
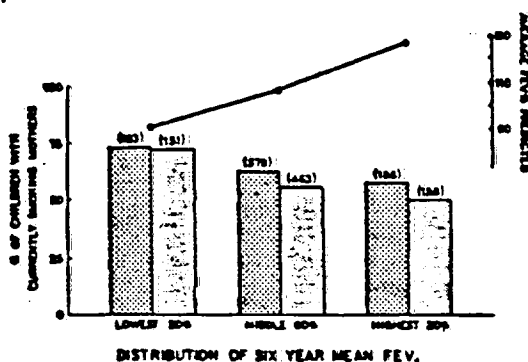
DISTRIBUTION OF SIX YEAR MEAN FEV₁

Figure 1. Percentage of Children with Mothers Who Were Current Cigarette Smokers at the Initial (Large Dots) and Sixth (Small Dots) Examinations, According to the Distribution of Mean Age, Height, and Sex-Corrected FEV₁ over the First Six Examinations.

"Lowest 20%," "middle 60%," and "highest 20%" refer to children with values in the bottom one fifth, middle three fifths, and upper one fifth, respectively, of the distribution of mean FEV₁. Numbers in parentheses indicate the number of children in each group. The three circles above the graph represent the average per cent predicted values of FEV₁ for the three groups. The results for male and female children were combined, since there was no significant difference between the sexes.

based on the model, are given in Table 3. The model predicted that over a two-year period, a nonsmoking male child with a currently smoking mother would accrue a 488-ml increase in FEV₁, as compared with a 539-ml increase if the mother did not smoke. Over a five-year period, the child was predicted to accrue a 1335-ml increase in FEV₁, as compared with a 1436-ml increase if the mother did not smoke. If the child also smoked, then the accrued FEV₁ was predicted to be only 315 ml over two years and 993 ml over five years. Removal of the effect of maternal smoking from that of a child who smoked was predicted to result in an increase of 366 and 1094 ml of FEV₁ over two and five years, respectively, as compared with expected increases of 539 and 1436 ml.

A similar analysis was carried out for FEF_{25-75}, but

Table 2. Regression Model Relating Change in FEV₁ over a One-Year Period to Mother's and Child's Smoking Status, after Correction for Initial FEV₁, Age, Sex, Height, and Change in Height.*

Variable	Regression Coefficient	Standard Error	P Value (Two-Tailed)
Intercept	−1.3390	0.0876	—
Initial level of FEV₁ (liters)	0.8389	0.0154	<0.001
Age (yr at time 0)	−0.0099	0.0036	0.006
Sex (1 = male)	0.0343	0.0112	0.002
Height (cm at time 0)	0.0443	0.0053	<0.001
Change in height in 1 yr (cm)	0.0436	0.0107	<0.001
Child's smoking status †	−0.0944	0.0278	<0.001
Mother's smoking status ‡	−0.0278	0.0114	0.015

*A total of 1657 person-years of observation were available for this model. The one-year period is denoted as 0-1) to (0.
†Most children listed as "ever" were current smokers — i.e., they had smoked in the interval before the last examination. Analysis using the same coding rubric as that used for mother's smoking status gave identical results.
‡Status in interval before last examination: 0 = nonsmoker or exsmoker; 1 = current smoker.

461 fewer person-years of observation were available than for the FEV₁ analysis, because current standards¹ permit the calculation of FEV₁ from a tracing that does not give a valid measurement of FEF_{25-75}. The effect of the mother's smoking status on FEF_{25-75} was in the same direction as its effect on FEV₁, but the difference was not statistically significant after correction for the other variables in Table 2 ($\beta = -0.0366$, $P = 0.174$).

In a comparison of households in which the mother was or was not a current smoker, there was no significant difference ($P = 0.173$) in the percentage of mothers who had completed high school (used as a crude measure of socioeconomic status; 115 of 235, or 48.9 per cent, vs. 76 of 135, or 56.3 per cent, respectively, on the basis of information obtained at the initial examination). Furthermore, the use of gas stoves for cooking (used as a measure of potential indoor environmental confounding factors) was significantly more common in households with mothers who did not smoke than in those with mothers who did (28 of 133, or 21.1 per cent, vs. 20 of 163, or 12.3 per cent; $\chi_1^2 = 4.158$, $P = 0.041$; for households present at the end of the seventh examination, the first year these data were obtained).

Table 3. Effect of Child's and Mother's Cigarette-Smoking Habit on Expected Rate of Growth in FEV₁ over a Five-Year Period, Based on the Autoregressive Model.*

Child's Smoking †	Mother's Smoking ‡	Expected Rate of Growth in FEV₁ (ml)		
		After 1 yr	After 2 yr	After 5 yr
No	No	262	539	1436
Yes	No	168 (64.1)	366 (67.9)	1094 (76.2)
No	Yes	234 (89.3)	488 (90.5)	1335 (93.0)
Yes	Yes	140 (53.4)	315 (58.4)	993 (69.2)

*The projected growth rates are for a male child who starts with population-median values for FEV₁ (1.93 liters), age (11 years), height (146 cm), and change in height (5 cm per year). Figures in parentheses indicate the percentage of increase in the level in a nonsmoking child of a currently nonsmoking mother.
†"No" denotes had never smoked, and "yes" had ever smoked.
‡"No" denotes former smoker or never smoked, and "yes" current smoker.

Discussion

Passive exposure to parental cigarette smoking is associated with an increase in morbidity from respiratory illness in young children.[14-23] Recently, several studies have sought to identify the direct effects of passive exposure to cigarette smoke on lung function in children. Cross-sectional data on the present cohort[1,2] indicate that parental cigarette smoking, especially maternal smoking, is associated with lowered levels of lung function in children as young as five to nine years. Several other studies have tended to confirm these observations. In a cross-sectional study of 16,689 symptom-free children, Hasselblad and colleagues[5] demonstrated that maternal cigarette smoking (number of packs smoked) was a significant predictor of the level of $FEV_{0.75}$. Paternal smoking had little predictive value. A cross-sectional analysis of

4061 children in grades one through six[4] also demonstrated an effect of parental cigarette smoking on the level of FEF_{25-75}. As in our prior study,[1] these authors found no effect on FEV_1 or forced vital capacity. The greatest effect was observed in female children with mothers who smoked. Initially, Speizer et al. found no effect of parental smoking[24]; however, subsequent analysis[5] has shown that children of mothers who smoke have significantly lower levels of FEV_1 than do children with mothers who do not smoke. In a study of children examined on two occasions over an average of 15 years, Higgins et al.[6] observed that pulmonary function was related to parental smoking history. Studies of adults in an industrial setting[25] and in households[26] have shown that passive exposure to cigarette smoking has small effects on lung function; however, the health implications of some of these findings have been called into question.[27]

Several investigators have failed to establish any relation between parental cigarette smoking and lung function in children. In a cross-sectional study of children, Schilling and colleagues[28] found no significant effect of passive smoking on the levels of $V_{max\ 50}$ and $V_{max\ 25}$ (maximal flow when 50 and 75 per cent of the forced vital capacity had been expired), although they did observe that the levels were lowest in girls with mothers who smoked. However, when their analysis was restricted to children who had never smoked, the levels of $V_{max\ 50}$ were significantly reduced in children with mothers who smoked. Since these authors used $V_{max\ 50}$ and $V_{max\ 25}$, which have a greater degree of variability than FEV_1, their study population may have been too small to detect an effect in all groups of children.[29] Nonetheless, these data are not dissimilar to those of Schenker et al.[4] Dodge[30] failed to find any effect of parental smoking on changes in lung function in children studied over a four-year period, but this investigation used relatively insensitive analytic techniques. Finally, Lebowitz et al.[31] observed that after correction of children's lung function for the age and the body mass of their parents and for the children's body mass, there was no correlation between Z scores for lung function in children and parents. However, it is likely that this analysis was too insensitive to detect any effects of parental smoking, since the numbers were very small (the largest number of subjects in any group was 96).

Our longitudinal study detected a significant effect of maternal cigarette smoking on the change in a child's FEV_1, after controlling for the previous level of FEV_1, age, sex, height, change in height, and the child's personal cigarette-smoking habit. The data in Table 3, which suggest that after five years, the lungs of nonsmoking children with mothers who smoke grow at only 93 per cent of the rate of growth in nonsmoking children with mothers who do not smoke, are certainly plausible in terms of the magnitude of the effect that one might predict for an environmental pollutant such as cigarette smoke. The size of the effect is consistent with that hypothesized to be sufficient as an

underlying risk predictor for obstructive airways disease in adult life.[32] Among the subjects in our analysis, socioeconomic status (assessed as maternal education) and exposure to gas cooking stoves did not appear to be responsible for the observed association between maternal smoking habit and rate of growth of lung function.

It is possible that the effect of maternal smoking — at least in the postnatal period — is indirect. For example, there is an increased occurrence of acute respiratory illness in the children of mothers who smoke, as compared with the children of mothers who do not.[14-23] Most of this effect has been observed during the first two years of life — a time when the lung may be particularly vulnerable to the long-term adverse consequences of such illnesses.[33,34] Thus, the observed effects of maternal cigarette smoking may be the consequence of structural changes that result directly from acute lower-respiratory illness early in childhood or indirectly from the long-term consequences of alterations in airway reactivity that may result from such illnesses.[34,35]

Our study also shows that smoking habits in children have a substantial negative effect on the rate of increase in FEV_1. A similar negative effect was also observed in the analysis of FEF_{25-75} ($P = 0.058$). These results reinforce the already existing body of cross-sectional data suggesting that even a relatively low level of direct tobacco exposure in children and adolescents has measurable effects on pulmonary function.[36-38]

In summary, these data suggest that maternal smoking contributes to a reduction in the rate of development of lung function in children and, along with the child's own smoking habits, may be important in the development of chronic obstructive disease of the airways in adult life.

Addendum: Since submission of this manuscript, we have developed an algorithm to compute the parameter estimates given in Table 2, with adjustment for the intraclass correlation between children in the same households. The results of the analysis are essentially unchanged (mother's smoking = −0.0203, $P = 0.03$). The algorithm is available from the authors upon request.
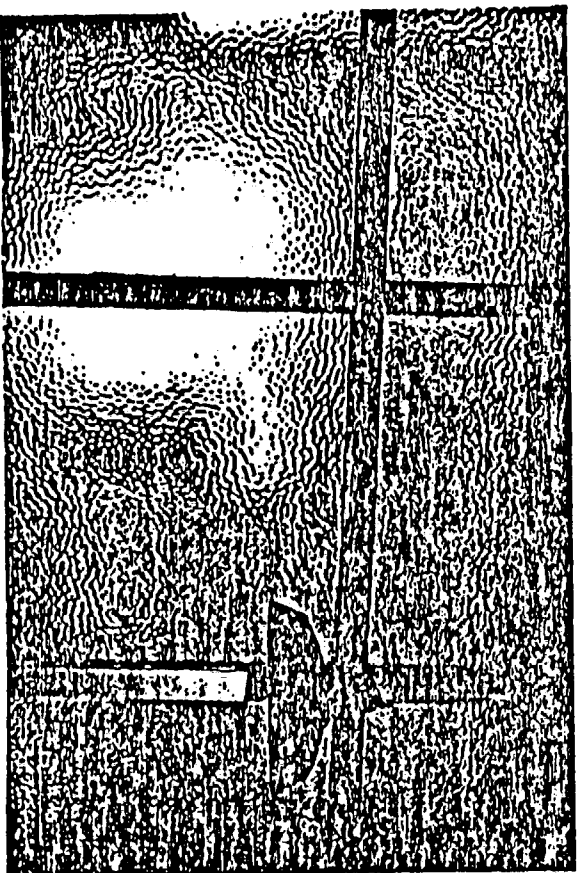
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ABSTRACT. We investigated the effects of maternal cigarette smoking
on pulmonary function in a cohort of children and adolescents
observed prospectively for seven years. A multivariate analysis
revealed that after correction for previous forced expiratory volume
in one second (FEV1), age, height, change in height, and cigarette
smoking in the child or adolescent, maternal cigarette smoking
significantly lowered the expected average annual increase in FEV1
(P=0.015). On the basis of this analysis, it is estimated that if
two children havve the same initial FEV1, age, height, increase in
height, and personal cigarette-smoking history, but the mother of
one has smoked throughout the child's life whereas the mother of
the other has not, the difference in the change in FEV1 over time
in the exposed child, as compared with that in the unexposed child,
will be approximately 28, 51, and 101 ml after one, two, and five
years, respectively, or a reduction of 10.7, 9.5, and 7.0 percent,
respectively, in the expected increase. These results suggest
that passive exposure to maternal cigarette smoke may have important
effects on the development of pulmonary function in children.

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Tashkin, D.P., Clark, V.A., Simmons, M., Reems, C., Coulson, A.H., Bourque, L.B., Sayre, J.W., Detels, R., Rokaw, S. "The UCLA Population Studies of Chronic Obstructive Respiratory Disease VII. Relationship between Parental Smoking and Children's Lung Function" Am Rev Respir Dis 129: 891-897, 1984.

SUMMARY: Results of previous studies of the impact of parents' smoking on children's lung function have been conflicting. To evaluate further the effect of passive smoking on the lung function of children, we analyzed respiratory questionnaire and lung function results obtained during field testing of residents (aggregated according to household) of 4 census tracts in the Los Angeles area. We report here on 971 white, non-Hispanic, nonsmoking, nonasthmatic children residing in households in which the smoking status of both parents was known; households with ex-smoking parents were excluded from analysis. We divided these children into 3 categories related to parental smoking status: (1) at least mother smokes, (2) only father smokes, and (3) neither parent smokes. Prediction equations for several indexes of forced expired volume and flow were derived separately for boys and girls 7 to 17 yr of age. Analysis of variance was used to compare lung function residuals of children in the 3 different passive smoking categories. Analysis was performed separately on younger (7 to 11 yr of age) and older (12 to 17 yr of age) children of each sex. Among younger male children, residual values were significantly lower in the maternal smoking category than in the other 2 household categories for maximal flow and maximal flow after exhalation of 25% of forced vital capacity (FVC) ($p < 0.05$); no differences were noted between the paternal-smoking only and nonsmoking household categories. A trend toward similar results was found in older male children, which approached significance ($p < 0.1$). Among females, forced expiratory flow during the middle half of the FVC and maximal flow after exhalation of 75% of FVC were significantly lower in relation to maternal smoking in the older children only ($p < 0.05$). ANOVA revealed no decrement in lung function in relation to passive smoking among children with asthma or bronchitis ($n+138$). No differences were noted by chi-square analysis in the frequency of any respiratory symptom comparing children in the different passive exposure categories. We conclude that passive exposure to at least maternal smoking (but not to paternal smoking alone) affects the airways of younger boys. The apparent effect on the lung function of heavily exposed older girls is more likely to be confounded by selective underreporting of "active smoking."

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The UCLA Population Studies of Chronic Obstructive Respiratory Disease

VII. Relationship between Parental Smoking and Children's Lung Function[1-3]

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Introduction

Habitual inhalation of the combustion products of tobacco is known to adversely affect the health of active (voluntary) smokers (1). Considerably less is known about how tobacco smoke affects the health of involuntarily exposed nonsmokers. Regular tobacco smoking produces readily detectable alterations in the structure and function of the respiratory tract of active smokers. Sidestream smoke contains many of the same constituents found in the smoke inhaled by voluntary smokers. Thus, the frequent involuntary inhalation of air contaminated by tobacco smoke may produce qualitatively similar, but quantitatively fewer, alterations in the lungs of passive smokers. The extent of such changes would be expected to depend on a number of factors. These include (1) the intensity of exposure, which is a function of characteristics of the environment (e.g., room volume and ventilation), the number of cigarettes smoked per unit time, proximity to the source of cigarette smoke, and the ratio of sidestream to exhaled, mainstream smoke; and (2) the characteristics of the person exposed (e.g., inherent airways sensitivity to constituents of tobacco smoke, and age). Because younger children have immature lungs, less immunity to respiratory infections, and a greater minute ventilation relative to body weight, they may be more vulnerable to adverse pulmonary effects of passive smoking.

Previous studies have investigated possible effects of passive smoking on the occurrence of respiratory infections and symptoms in infants and children with variable results. A relationship has been found between parental smoking and the incidence of lower respiratory illness in children, but only or mainly during the first year of life (2-7). Children exposed to parental smoking have been found to have a greater frequency of respiratory symptoms than unexposed children (8-11). However, in some studies (8-10), this difference was no longer significant when adjustment was made for parents' respiratory symptoms, possibly reflecting transmission of infection to children or a bias towards reporting symptoms by symptomatic parents. In contrast, an apparent dose-dependent relationship was found between parental smoking and persistent wheeze in children, which was independent of the presence of wheezing in either parent (11).

Studies of the relationship between parental smoking and children's lung function have also yielded variable results. Schilling and coworkers (10) failed to find any significant relationship between parents' smoking and

SUMMARY Results of previous studies of the impact of parents' smoking on children's lung function have been conflicting. To evaluate further the effect of passive smoking on the lung function of children, we analyzed respiratory questionnaire and lung function results obtained during field testing of residents (aggregated according to household) of 4 census tracts in the Los Angeles area. We report here on 971 white, non-Hispanic, nonsmoking, nonasthmatic children residing in households in which the smoking status of both parents was known; households with ex-smoking parents were excluded from analysis. We divided these children into 3 categories related to parental smoking status: (1) at least mother smokes, (2) only father smokes, and (3) neither parent smokes. Prediction equations for several indexes of forced expired volume and flow were derived separately for boys and girls 7 to 17 yr of age. Analysis of variance was used to compare lung function residuals of children in the 3 different passive smoking categories. Analysis was performed separately on younger (7 to 11 yr of age) and older (12 to 17 yr of age) children of each sex. Among younger male children, residual values were significantly lower in the maternal smoking category than in the other 2 household categories for maximal flow and maximal flow after exhalation of 25% of forced vital capacity (FVC) ($p < 0.05$); no differences were noted between the paternal-smoking only and nonsmoking household categories. A trend toward similar results was found in older male children, which approached significance ($p < 0.1$). Among females, forced expiratory flow during the middle half of the FVC and maximal flow after exhalation of 75% of FVC were significantly lower in relation to maternal smoking in the older children only ($p < 0.05$). ANOVA revealed no decrement in lung function in relation to passive smoking among children with asthma or bronchitis ($n = 138$). No differences were noted by chi-square analysis in the frequency of any respiratory symptom comparing children in the different passive exposure categories. We conclude that passive exposure to at least maternal smoking (but not to paternal smoking alone) affects the airways of younger boys. The apparent effect on the lung function of heavily exposed older girls is more likely to be confounded by selective underreporting of "active smoking." AM REV RESPIR DIS 1984; 129:891-897

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several indexes of lung function derived from timed spirometry in boys 7 to 17 and girls 7 to 14 yr of age, except for maximal flow after exhalation of 50% of forced vital capacity ($Vmax_{50}$) in girls in households where only the mother smoked. On the other hand, Tager and associates (12) detected a clear trend toward an inverse relationship between the level of predicted forced expiratory flow during the middle half of the forced vital capacity (FEF_{25-75}) as a ranked score in children 5 to 9 yr of age and the number of smoking parents in the household, although this relationship was not statistically significant. The discrepancy in findings between these 2 groups of investigators may be explained by differences in the study populations, the actual levels of exposure to passive smoking, and/or the methods of analysis.

In view of the conflicting findings of previous workers concerning the possible impact of passive exposure to sidestream smoke on respiratory symptoms and lung function of nonsmoking children, we further evaluated this question by analyzing respiratory questionnaire and lung function data collected during field testing of residents (aggregated according to household) of 4 census tracts in the Los Angeles area.

Methods

A cohort study of chronic obstructive respiratory disease has been under way in 4 selected areas of Los Angeles County since 1973 (13-17). The areas were selected to be homogeneous in demographic characteristics, and heterogeneous across sites in historical exposure to different levels and types of atmospheric pollutants. All 4 areas are predominantly white and middle class. Residents in over 90% of households in each area were enumerated. All persons 7 yr of age and older were invited to be interviewed and undergo lung function testing in a mobile laboratory located in the selected areas. The interview schedule consisted of a modified National Heart, Lung and Blood Institute questionnaire (13, 14) and provided demographic data and information on symptomatology, respiratory and allergic disease history, smoking behavior (present and past cigarette use, pipe and cigar consumption), history of occupational exposure to hazardous substances, and residence history. Responses of children 12 yr of age or younger to questions concerning smoking behavior were not thought to be reliable under the conditions of this study in which younger children usually accompanied their parents to the mobile laboratory; therefore, these children were all assumed to be nonsmokers. Although similar reservations were held concerning the reliability of responses of teenage children to the same questions, the older children were asked to respond to these questions. Usually (but not always), the teenage children's parents were not present during the interview. Lung function measurements included tests of forced exhalation (timed spirometry, maximal expiratory flow-volume curves), single-breath nitrogen washout, and whole body plethysmography (airway resistance, thoracic gas volume at functional residual capacity, and specific airway conductance). Data reported in this study were collected between 1973 and 1977 during the first round of testing in each of the 4 study areas.

Households with children 7 to 17 yr of age were identified from the household rosters. Only households in which one or both parents were regular smokers or lifetime nonsmokers were included in the analysis. Households in which one or both parents were former smokers were excluded because of wide variability in the duration of abstinence from tobacco among ex-smoking parents and, hence, in the passive smoking exposure of their children. Households with nonparent adults who were regular or former smokers or whose smoking status was unknown were excluded from analysis, except if both parents in the household were already regular smokers (see below). Regular cigarette smokers were defined as persons who reported that they currently smoked more than 1 cigarette per day on a regular basis and had done so for at least 1 yr. Nonsmokers were defined as those who had *never* smoked more than 1 cigarette per day on a regular basis for at least 1 yr. Only white children *without* a history of asthma, bronchitis, or other reported lung disease who did not indicate that they had ever smoked were included in the main analyses. White children *with* asthma or bronchitis who were self-reported never-smokers comprised a separate group for analysis.

Our sample was derived in the following manner. Households were excluded either because they failed to meet the stated criteria or because necessary information was missing on one or more household members. An enumerator visited 9,083 households. In 5,533 of these, all the members of the household 7 yr of age or older participated in the study. Twenty-seven percent of these households, or 1,476, had children in the 7- to 17-yr age range who underwent pulmonary function testing in the mobile laboratory. After excluding households with former smokers, and households that contained at least 1 nonparent adult who smoked (or whose smoking status was unknown) in an otherwise nonsmoking household or in one where only one parent smoked, 840 households with 1,472 children were eligible for study. Children were excluded who were nonwhite or had a Spanish surname. In addition, children who were known ever-smokers or had physician-diagnosed asthma, bronchitis, or other reported lung disease, were excluded from the main analysis. This left 1,160 children for study. An additional 189 children were excluded because questionnaire or lung function data were incomplete and/or missing, or because their maximal expiratory flow-volume curves were technically unsatisfactory. A total of 971 children from 615 households were thus eligible for study. These children represent 28% of all children 7 to 17 yr of age in the study cohort and 66% of such children who resided in households that were eligible for study. An additional 138 white, reportedly never-smoking children *with* a physician-diagnosis of asthma or chronic bronchitis were analyzed separately.

Analyses reported here, therefore, are for 3 types of households: (1) at least mother smokes, (2) only father smokes, and (3) no one smokes. In all analyses, age, height, and area were controlled for in a linear fashion. Analyses were also performed separately for male and female children and for 2 age-defined subgroups of children: those 7 to 11 and those 12 to 17 yr of age. This latter subdivision was made for 2 reasons. First, it was desirable to see if younger or older children were more affected by parental smoking. Second, although no children were included in the analyses who were self-reported smokers, there was concern that some teenagers who actually smoked might not report their smoking to an interviewer. Families often came together to the mobile function laboratory and the members were processed consecutively. Knowing that their parents were nearby might have influenced some teenage smokers to say that they did not smoke. On the other hand, younger children (even though not questioned as to their smoking behavior) are much less likely to smoke, particularly in these middle-class areas (1).

Linear regression equations predicting each of 7 indexes of lung function were run separately for male and female children: FVC, forced expiratory volume in one second (FEV_1), FEF_{25-75}, Vmax, V_{50}, V_{25} and V_{75}. Age, height, and geographic area (dummy variable) were entered as predictor variables. These equations were obtained for children without self-reported chronic lung disease who came from households where everyone was nonsmoking. Residuals were calculated for all male and female children, using the appropriate equation, regardless of the smoking status of their parents. One-way analysis of variance (18) was used to test whether residual lung function results by sex were equal in the 3 types of households. Mean residual levels are set at zero for children who came from nonsmoking households (who were used to define the equations). The size of the mean residual for the other 2 groups is an indicator of the effect parental smoking has on these children. One-way analyses of vari-

TABLE 1

NUMBER OF CHILDREN 7 TO 17 YR OF AGE
BY HOUSEHOLD TYPE

Household Type	Male Children (m)	Female Children (n)	Overall (n)
At least mother smokes	207	200*	407†
Only father smokes	99	93*	192
Everyone nonsmoking	190*	182*	372
Total	496	475	971

* For FEF_{25-75}, Vmax, V_{50}, V_{25}, and V_{75}, males n = 188 (everyone nonsmoking), females n = 198 (at least mother smokes), n = 92 (only father smokes), and n = 180 (everyone nonsmoking). For definition of abbreviations, see table 2.
† Of the 407 children whose mother smokes, 276 come from households where both parents smoke, and 131 come from households where the father does not smoke.

ance also were performed on residuals across household types within the 2 age groups (7 to 11 and 12 to 17 yr of age). Mean residual levels for children from nonsmoking households within these separate groups will not necessarily be zero because prediction equations were based on data from both age groups combined. These same analyses were repeated, using one-way analysis of covariance, where age, height, and geographic area were entered as covariates.

In our analyses, which assume independent observations, we did not adjust for sibship size. Therefore, a portion of our observations lacks independence. However, because our data were analyzed separately by sex, this portion is not large, 23% for males and 20% for females. Moreover, when the data are further divided into age groups 7 to 11 and 12 to 17 yr of age, the portion of the households that contributes more than one child to each analysis is even less. Therefore, our analyses were for the most part based on independent observations.

For those lung function results in which the analysis of variance indicated a significant difference among the mean residual levels for the 3 types of households, linear contrasts were performed (19). Two contrasts were uniformly performed. First, the means for nonsmoking households were contrasted with those for households where only the father smoked. Second, the means for households where at least the mother smoked were contrasted with the pooled means of the other 2 household categories. The significance level, or p value, is presented using the *t* test. This p value is compared to an α of 0.025 for an overall level of significance of 5% for 2 contrasts, or 0.05 if only 1 contrast is considered (19). In accordance with standard reporting procedures, the significance levels we used

apply only to 1 lung function test for each set separately, not across all lung function tests.

Prevalence of each type of respiratory symptom (cough, sputum, increased cough and sputum, wheezing, breathlessness, acute chest illness) or of *any* respiratory symptom among children from the 3 types of households was compared using chi-square or Fisher's exact test (20). Individual children were judged to have a positive history for each of the above symptoms according to previously published criteria (13, 14).

Results

A total of 971 children 7 to 17 yr of age were studied in the 4 geographical areas. The number of male and female children in each of the 3 types of households is given in table 1. Thirty-eight percent of the children resided in households in which no one reported smoking. If only one parent smoked, 59% of the time it was the father. Over 90% of the smoking parents started smoking before the birth of the oldest of their children included in our analysis. The average ages and heights of the children were very similar by type of household.

The mean values of adjusted lung function obtained from covariance analysis, lung function residuals, and the results of the analyses of variance computed on the residuals across household types within sex are reported in table 2. For male children 7 to 17 yr

TABLE 2

ADJUSTED MEAN VALUES OF CHILDREN'S LUNG FUNCTION,* RESIDUAL LUNG FUNCTION,†
AND SIGNIFICANCE LEVELS,† BY HOUSEHOLD TYPE AND SEX OF CHILD

Lung Function Test, Unit	Male Children			Female Children			Overall Mean		Level of Significance†	
	At Least Mother Smokes	Only Father Smokes	Everyone Non-smoker	At Least Mother Smokes	Only Father Smokes	Everyone Non-smoker	Males	Females	Males	Females
Adjusted mean lung function*										
FVC, L	2.84	2.92	2.96	2.54	2.57	2.53	2.90	2.54		
FEV_1, L	2.41	2.51	2.50	2.20	2.26	2.21	2.47	2.22		
FEF_{25-75}, L/s	2.72	2.90	2.88	2.67	2.88	2.74	2.82	2.74		
Vmax, L/s	5.65	6.10	6.01	5.26	5.46	5.31	5.88	5.32		
V_{50}, L/s	4.45	4.92	4.80	4.36	4.55	4.34	4.68	4.39		
V_{25}, L/s	3.12	3.28	3.34	3.15	3.43	3.21	3.23	3.23		
V_{75}, L/s	1.54	1.67	1.62	1.50	1.66	1.59	1.60	1.56		
Mean residual lung function†										
FVC, L	-0.101	-0.043	0.000	0.032	0.049	0.000			0.12	0.61
FEV_1, L	-0.064	0.004	0.000	0.007	0.065	0.000			0.08	0.29
FEF_{25-75}, L/s	-0.143	0.025	0.000	-0.097	0.118	0.000			0.10	0.05
Vmax, L/s	-0.369	0.066	0.000	-0.029	0.167	0.000			0.004	0.37
V_{50}, L/s	-0.362	0.104	0.000	0.036	0.225	0.000			0.003	0.19
V_{25}, L/s	-0.213	-0.066	0.000	-0.067	0.212	0.000			0.06	0.03
V_{75}, L/s	-0.076	0.046	0.000	-0.103	0.057	0.000			0.17	0.05

Definition of abbreviations: FVC = forced vital capacity; FEV_1 = forced expiratory volume in one second; FEF_{25-75} = forced expiratory flow during the middle half of the FVC; Vmax = maximal flow; V_{50}, V_{25}, and V_{75} = maximal flow after exhalation of 25, 50, or 75% of FVC.
* From analysis of covariance, using age, height, and area as covariates.
† From analysis of variance on residuals, calculated from linear regressions obtained in children from nonsmoking households, using age, height, and area as the independent variables.

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of age, highly significant differences ($p < 0.004$) were found for indexes of large airways function (Vmax and V_{50}); a difference of borderline significance ($p = 0.061$) was noted for V_{50}. For female children, significant differences ($p < 0.05$) were found only for indexes of small airways function (V_{50} and V_{75}), the difference for FEF_{25-75} approaching significance ($p = 0.052$). Results similar to those reported in table 2 from the ANOVA on the residuals were obtained from the covariance analyses.

Linear contrasts were performed on all lung function tests for which the analysis of variance yielded significant differences. The lung function of children in the "only father smokes" category, although higher on the average than that of children in the nonsmoking households, was not significantly different from the latter. Comparing the households where at least the mother smoked to the combined average of those where only the father smoked or no one smoked, significant differences did exist. For male children, the levels of significance were $p < 0.001$ for Vmax and V_{50}. Female children from households where the mother smoked had a significantly lower residual for V_{75} ($p < 0.02$) and a lower residual of borderline significance for V_{50} ($p = 0.035$) than children in the other household categories. These p values should be compared to an α level of 0.05/2, or 0.025, because 2 contrasts were made for each analysis (20).

To assess the magnitude of the difference in lung function for children from households where the mother smoked, the percent reduction in mean values was calculated (table 3). The largest reduction for male children is seen in V_{50} (7.7%) and for female children in V_{75} (6.6%).

In tables 4 and 5, results similar to those presented in table 2 are reported separately for children 7 to 11 for children and 12 to 17 yr of age. There were no significant differences between household types in the slopes of the pulmonary function variables regressed against height and age for the different age-sex groups. For male children 7 to 11 yr of age (table 4), significant differences ($p < 0.03$) were again found for Vmax and V_{25}, as well as for V_{50} ($p < 0.04$). Among the older male children, however, no significant differences across household categories were noted for any lung function test, although the results for Vmax and V_{25} approached significance ($p < 0.1$). Note that the sample sizes for the separate age groups are smaller, so that it takes a larger mean difference to obtain significance. The results from the linear contrasts failed to demonstrate any significant differences between the nonsmoking households and those where only the father smoked for any test of lung function. Contrasting the lung function results for households where the mother smoked versus the other 2 categories of households for male children 7 to 11 yr of age, significant differences were found for Vmax ($p < 0.02$) and V_{25} ($p < 0.005$).

For the female children (table 5), no significant differences were noted among those 7 to 11 yr of age, whereas FEF_{25-75}, V_{50}, and V_{75} were significant ($p < 0.032$) for those 12 to 17 yr of age. The contrasts for V_{75}, V_{50}, and FEF_{25-75} for the older females indicated no significant differences between the means when nonsmoking households were compared with those where only the father smoked. In comparing the households where the mother smoked with the average of the other two, significant differences were found for V_{75} ($p < 0.005$) and FEF_{25-75} ($p < 0.02$), and the difference for V_{50} approached significance ($p < 0.05$).

To evaluate the possibility that quantity of parental cigarette smoking may be an important determinant of the relationship between passive exposure to tobacco smoke in the household and children's lung function, we regressed lung function residuals of children against the number of cigarettes currently smoked by their mothers (in "at least mother smokes" households) or their fathers (in "only father smokes" households). The results of these analyses failed to reveal any significant correlation between children's lung function and the quantity of tobacco smoked by their parents among either male or female children in either parent-smoking household category.

To assess the effects of passive smok-

TABLE 3

PERCENT REDUCTION IN MEAN LUNG FUNCTION AMONG CHILDREN IN FAMILIES WHERE AT LEAST MOTHER SMOKES

Lung Function Tests	Males	Females
FVC	-3.5*	1.3
FEV_1	-3.4	0.3
FEF_{25-75}	-5.1	-3.5
Vmax	-6.3	-0.5
V_{50}	-7.7	0.8
V_{25}	-6.6	-2.1
V_{75}	-4.8	-6.6

For definition of abbreviations, see table 2.
* Represents ratio of mean residual lung function value to adjusted overall mean value, expressed as percent.

TABLE 4

ADJUSTED MEAN LUNG FUNCTION VALUES,* MEAN RESIDUAL LUNG FUNCTION VALUES,† AND SIGNIFICANCE LEVELS† FOR MALE CHILDREN, BY HOUSEHOLD TYPE AND AGE GROUP

Lung Function Test	Ages 7 to 11 Yr				Ages 12 to 17 Yr			
	At Least Mother Smokes	Only Father Smokes	Everyone Non-smoker	Significance Level	At Least Mother Smokes	Only Father Smokes	Everyone Non-smoker	Significance Level
Adjusted mean levels								
FVC	1.95	2.01	2.05		3.65	3.73	3.77	
FEV_1	1.66	1.72	1.72		3.08	3.20	3.20	
FEF_{25-75}	1.94	2.05	2.03		3.43	3.65	3.62	
Vmax	3.96	4.17	4.22		7.20	7.74	7.57	
V_{50}	3.17	3.45	3.44		5.64	6.16	5.98	
V_{25}	2.26	2.34	2.47		3.88	4.10	4.10	
V_{75}	1.13	1.13	1.14		1.91	2.13	2.05	
Mean residual levels								
FVC	-0.070	0.031	0.044	0.10	-0.130	-0.102	-0.040	0.51
FEV_1	-0.043	0.060	0.036	0.09	-0.123	-0.041	-0.033	0.37
FEF_{25-75}	-0.083	0.085	0.051	0.18	-0.199	-0.022	-0.045	0.37
Vmax	-0.280	0.086	0.112	0.03	-0.451	0.050	-0.099	0.08
V_{50}	-0.347	0.076	0.070	0.01	-0.376	0.126	-0.062	0.10
V_{25}	-0.198	-0.060	0.054	0.04	-0.227	-0.070	-0.047	0.45
V_{75}	-0.000	0.059	0.031	0.74	-0.147	0.036	-0.026	0.21
Number of children	100	44	90‡		107	55	100	

For definition of abbreviations, see table 2.
* From analysis of covariance, using age, height, and area as covariates.
† From analysis of variance on residuals, calculated from linear regressions obtained in children from nonsmoking households, using age, height, and area as the independent variables.
‡ Eighty-eight for FEF_{25-75}, Vmax, V_{50}, V_{25}, V_{75}.

ing on children with asthma or bronchitis ($n = 138$), who were excluded from the main analysis described above, a separate analysis of variance similar to that reported in table 3 was performed on their residual values. No significant differences were found among the male asthmatic and bronchitic children ($n = 78$) across household categories. Among the female children with asthma or bronchitis ($n = 60$), significant differences ($p < 0.02$) were found for FEF_{25-75} and V_{50}; for both of these tests of lung function, however, the children from nonsmoking households had the lowest residuals, and those from households where only the father smoked had the highest. Prevalence of asthma among children did not differ across the different household categories.

For nonasthmatic, as well as asthmatic, children, no significant differences were found in the number of either males or females reporting any *particular* symptom (or *any* symptom) by household type (chi-square test for independence or Fisher's exact test).

Discussion

The present study indicates that passive exposure to at least maternal smoking is associated with reduced lung function in nonsmoking children, but is not related to the occurrence of chronic respiratory symptoms in children. Paternal smoking alone, on the other hand, was not associated with any decrement in children's lung function or with prevalence of respiratory symptoms. One possible, but unproved, explanation for these findings is that children may be more intensively exposed to smoking by the mother, who is more likely to spend more time in the home, especially during the early life of her children, and thus to contribute more to indoor smoke pollution. To further explore this possibility, the work status of the mother was considered. A separate analysis of variance was performed wherein households in which only the mother smokes but works outside the home were contrasted with those in which only the mother smokes and does not work. These contrasts failed to reveal any significant differences in the residual lung function of either male or female children in either the younger or older age category. These findings, however, do not preclude the possibility that a mother's smoking—regardless of work status—has a greater impact on her children than paternal smoking, because even working mothers generally spend more time in the household involved in direct

child care activities than do fathers over the entire lifetime of their children.

Our observation of a significant relationship between maternal smoking and decrements in indexes of small airways function among girls 12 to 17 yr of age but not among those 7 to 11 yr of age is consistent with the possibility of either a selective adverse effect of passive smoking on older girls or, more likely, an "active" smoking effect (21) among older girls in the maternal smoking household category who might selectively be underreporting personal cigarette smoking. The latter possibility is suggested by our finding of an unexpectedly low prevalence of self-reported active smoking among teenage girls (12%), including those from smoking households.

In contrast, we observed a more consistent relationship between maternal smoking and decrements in lung function among male children both 7 to 11 yr of age and 12 to 17 yr of age; this relationship was significant for the younger boys and approached significance for the older male children. These findings suggest a passive smoking effect in boys exposed to maternal smoking. The fact that the decrements in lung function in the older male children in the maternal smoking household category did not achieve statistical significance could be due to greater variability in height- and age-adjusted lung function among older than among younger boys. This is consistent with our earlier finding that teenage boys are in the phase of lung growth where the most rapid rates of change in lung function are occurring (22). Moreover, "true" passive smoking effects in older male children might have been confounded and obscured if active smoking behavior were underreported by teenage boys to a comparable extent in all household categories. Finally, older male children from "at least mother smokes" households may be subjected to less passive exposure to maternal smoking than are younger boys because of differences in the proportion of time spent in the house after school. On the other hand, the discrepancy in the apparent effect of passive smoking on younger male versus younger female children is unlikely to be due to differences in involuntary exposure to second-hand smoke because, if anything, boys are less likely than girls to be exposed to maternal smoking in the household because of differences in indoor-outdoor play activities. This

TABLE 5

ADJUSTED MEAN LUNG FUNCTION VALUES,* MEAN RESIDUAL LUNG FUNCTION VALUES,† AND SIGNIFICANCE LEVELS‡ FOR FEMALE CHILDREN, BY HOUSEHOLD TYPE AND AGE GROUP

Lung Function Test	Ages 7 to 11 Yr				Ages 12 to 17 Yr			
	At Least Mother Smokes	Only Father Smokes	Everyone Non-smoker	Significance Level	At Least Mother Smokes	Only Father Smokes	Everyone Non-smoker	Significance Level
Adjusted mean levels								
FVC	1.92	1.94	1.86		3.15	3.17	3.16	
FEV_1	1.64	1.65	1.60		2.75	2.85	2.77	
FEF_{25-75}	2.00	2.02	2.00		3.31	3.68	3.43	
Vmax	3.92	4.13	3.88		6.55	6.70	6.67	
V_{50}	3.32	3.47	3.29		5.35	5.58	5.33	
V_{40}	2.39	2.50	2.37		3.87	4.29	4.02	
V_{75}	1.15	1.15	1.15		1.84	2.13	1.99	
Mean residual levels								
FVC	0.044	0.056	-0.018	0.47	0.020	0.044	0.019	0.94
FEV_1	0.017	0.023	-0.013	0.74	-0.002	0.099	0.013	0.25
FEF_{25-75}	-0.090	-0.075	-0.029	0.80	-0.103	0.274	0.030	0.02
Vmax	-0.031	0.153	-0.050	0.50	-0.026	0.178	0.051	0.64
V_{50}	-0.002	0.104	-0.047	0.66	0.071	0.322	0.049	0.31
V_{40}	-0.100	-0.002	-0.060	0.75	-0.035	0.384	0.064	0.03
V_{75}	-0.032	-0.037	-0.014	0.95	-0.169	0.132	0.014	0.01
Number of children	97	42‡	83‡		103‡	51	89‡	

For definition of abbreviations, see table 2.
* From analysis of covariance, using age, height, and area as covariates.
† From analysis of variance on residuals, calculated from linear regressions obtained in children from nonsmoking households, using age, height, and area as the independent variables.
‡ 41, 92, 102, and 88, respectively, for FEF_{25-75}, Vmax, V_{50}, V_{40}, V_{75}.

sex-related discrepancy in the younger children could possibly be due to inherently greater vulnerability of boys than girls to the injurious effects of inhaled respiratory irritants. The prevalence of asthma is greater in males from birth up to 16 yr of age (23). It is possible, therefore, that more boys than girls in our study sample had latent asthma. Such boys may have had relatively greater airways reactivity to the smoke contaminating their indoor environment, leading to a sustained deficit in lung function.

Our failure to observe a significant relationship between the current quantity of smoking by parents and the lung function residuals of their children suggests that other factors relating to parental smoking may have a more important influence on children's lung function. Such factors (not evaluated by us) could include variations in room ventilation, in previous levels of cigarette smoking by parents (when their children were younger), and in the smoking habits of parents in the presence of their children.

Factors that need to be considered as possible confounders of the relationship between parental smoking and children's respiratory status include variations across household categories in (1) the type and level of community air pollution, (2) non-cigarette-related indoor pollution (such as that caused by gas cooking) (24-26), (3) crowding, and (4) socioeconomic status. The households examined in this report were located in 4 geographically distinct areas of Southern California, which were selected because of their similarity in demographic distributions, including race, income, and home value, and their historical dissimilarity in type and/or level of atmospheric pollution: low levels of chemical pollutants (Lancaster), moderate to heavy levels of oxidant pollution (Burbank and Glendora, respectively), and moderately heavy levels of SO_2, hydrocarbons, and particulates (Long Beach). Cross-sectional comparisons of lung function of adults across these communities have shown significant differences in age-, height-, and sex-adjusted mean values for different indexes of lung function, the worst mean values being noted in the residents of the communities with the worst air pollution (Glendora and Long Beach) (16, 17).

In analyzing the relationship between parental smoking and children's lung function, we believe that possible effects of ambient air pollution on children's lung function were adequately controlled for through adjustment for the effects of area by using area as a dummy variable in our linear regression equations and as a covariate in our analyses of covariance. Moreover, the proportion of parent-smoking households was not significantly different across all 4 study areas and, if anything, was actually highest in our community with the cleanest air.

Although cigarette smoke probably constitutes the most important source of indoor air contamination, other indoor pollutants, particularly gas fuel used in cooking, might adversely affect lung function; studies of the impact of indoor exposure to cooking fuel on lung function, however, have yielded variable results (26, 27). Questions concerning the mode of indoor cooking were not asked of our subjects until the second round of testing in our cohort study. Data collected subsequently from 200 of the 615 households (33%) in our cohort indicate that during the lifetime of children included in the analysis, 102 households used gas fuel alone for cooking, 20 used electricity alone, and 78 had switched from one type of fuel to the other at least once. The proportion of households in which gas fuel alone was used for cooking was similar across parental smoking household categories. Moreover, using these data in a two-way analysis of covariance, we failed to find a significant effect of exposure to gas cooking fuel on lung function or any interactive effect of gas cooking and passive smoking on lung function.

Although the Hollingshead score for occupation of the head of household (an indicator of socioeconomic status) was related to household smoking status category, it showed no relationship to children's lung function, nor was there a significant interaction between the effect of household category and the Hollingshead score on children's lung function (two-way ANOVA). Parental level of education (another socioeconomic indicator), although significantly higher in nonsmoking households, did not correlate with children's residual lung function. The size of the families and the number of rooms in the residence were evenly distributed across household categories, decreasing the possibility that our results were confounded by any effects of crowding or of volume of dilution of

indoor pollutants on lung function. Although the exclusion of some children because of missing or technically unsatisfactory data could have biased our results, the observation that the proportion of such children was evenly distributed across household categories and that the excluded children were of a similar age and height to those of the children included in the analysis should have reduced these biases.

Even though the risk of chronic pulmonary alterations caused by passive tobacco smoke exposure may be relatively subtle and only variably demonstrable in the general population (10, 12, 27, 28), passive smoking might be expected to have more obvious respiratory consequences in asthmatics, who hyperreact to a number of noxious stimuli. In all 4 of our study areas, the prevalence of asthma or bronchitis was similar among children in the different household categories: at least mother smokes (11%), father only smokes (13%), and no parent smokes (10%). However, no relationship was apparent between parental smoking and either lung function or symptomatology of asthmatic boys; moreover, among female children with asthma, the lowest residuals were actually noted in those from households in which neither parent smoked, and this relationship was significant ($p < 0.02$). Although these unexpected findings do not support the hypothesis that parental smoking aggravates children's asthma (29), the exclusion of households with ex-smoking parents from our analysis could have biased our results.

Our finding of lower lung function in nonsmoking boys from households with at least maternal smoking is somewhat in accord with, and extends, the data of Tager and coworkers (12), who found a relationship between the smoking habits of parents and the midexpiratory flow rates of their children 5 to 9 yr of age. The latter investigators, however, did not examine the impact of parental smoking on male and female children separately, so that the trend they noted toward a decreasing level of function in children with increasing parental smoking might have been stronger or weaker if the results in boys and girls had been analyzed separately. Also, it would have been of interest if they had analyzed other indexes of lung function in addition to FEF_{25-75} because the strongest associations we noted were between parental smoking and the residuals for Vmax and V_{25} in

boys. Moreover, we excluded ex-smokers from analysis, whereas their definitions of parent-smoking households accepted parent ex-smokers as "current" smokers if they had smoked during the first year of life of all their children. Therefore, if passive smoking effects on children are influenced by persistent exposure to smoke contamination in the household beyond the first year of life, the effect of parental smoking noted by these investigators might have been underestimated.

On the other hand, our results are not in agreement with those of Dodge (27) or of Schilling and associates (10). Dodge was unable to demonstrate a significant relationship between the smoking of either Anglo-white or Mexican-American parents and the FEV_1 of their Arizona schoolchildren (27). In our study, we were also unable to find a significant relationship between the FEV_1 of children of either sex and the smoking of their parents, but this relationship approached significance in boys (p < 0.1). The discrepancy between our findings and those of Schilling and associates (10), who failed to find a significant contribution of parents' smoking to children's lung function in 3 towns in Connecticut, may be due to differences in sample sizes, types of lung function examined, or analytic techniques. Also, it is not clear how these investigators classify parent ex-smokers, who were excluded from our analysis. Classification of ex-smokers as either smokers or non-smokers could conceivably obscure significant differences between parent-smoking and lifetime nonsmoking households.

Although we found significantly lower values for V_{max} and V_{25} among boys in relation to maternal smoking, these decrements were, in fact, relatively small (e.g., 7.7%, or 0.37 L/s, decrease in V_{25}). Although these decrements were statistically significant, their biologic significance might be questioned. In this regard, it is note-worthy that the children we studied, especially the younger children, were undergoing a rapid rate of growth and development of their lungs. Consequently, the small difference in lung function we observed could be important if it interfered with the normal achievement of full lung growth, as previously suggested (26).

Acknowledgment

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Vedal, S., Schenker, M.B., Samet, J.M., Speizer, F.E. "Risk Factors
for Childhood Respiratory Disease: Analysis of Pulmonary Function"
American Review of Respiratory Disease 130:   187-192, 1984.

SUMMARY: Four thousand elementary-school-age children from a rural
area of western Pennsylvania participated in a cross-sectional
survey that consisted of a standardized respiratory questionnaire
completed by their parents and spirometric testing at school.
Spirographic tracings were digitized to obtain the FVC,
FEV0.75, FEF25-75, Vmax75, and Vmax90, which were standardized for
height, age, and sex for the subsequent analyses.   Independent
associations of potential risk factors with the standardized
pulmonary function measures were evaluated with multiple regression
techniques. Asthma, persistent wheeze, and parental smoking habits,
especially those of the mothers, were associated with lower flow
rates. The effect of parental smoking was primarily due to smoking
by the mother and was stronger in girls.   In female children of
currently smoking mothers, FEF25-75 was 96% of predicted, Vmax75
was 95% of predicted, and Vmax90 was 92% of predicted; each flow
measure was 98% of predicted in male children of smoking mothers.
Prolonged hospitalization at birth was independently associated
with lower FEV0.75 and flow rates.   Low socioeconomic status was
associated with lower FVC and FEV0.75.   Neither current gas stove
use nor a history of severe chest illness before 2 yr of age were
independently associated with lower levels of pulmonary function.

Risk Factors for Childhood Respiratory Disease

Analysis of Pulmonary Function[1-4]

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Introduction

The identification of risk factors for lower levels of pulmonary function in children may lead to specific strategies for early intervention. Of particular interest at present are the possible effects on children of exposure to gas stove fumes and to parental smoking (1). Also of continuing interest is the hypothesized relationship between childhood respiratory illness and the subsequent development of chronic air-flow obstruction in adult life (2). A decreased level of pulmonary function in children may influence susceptibility to tobacco smoke in adulthood. Because there is still lack of agreement on the factors that increase a child's risk for lower levels of pulmonary function, further characterization of risk factors in large population samples is needed.

As part of a series of studies investigating the health effects of air pollution in adults and children in the Chestnut Ridge region of western Pennsylvania, we have previously reported the results of parent-completed questionnaires for 4,071 children 5 to 14 yr of age (3). Predictors of respiratory symptoms and illnesses in this population included younger age, male sex, and low socioeconomic status (SES). Parental cigarette smoking was associated with chest illnesses in the children but not with chronic cough, phlegm production, or persistent wheeze. This report details findings from analysis of spirometric testing in the same sample of children.

Methods

Study Area and Population

The study area and study population have been previously described (3). Briefly, the area is a rural region of western Pennsylvania consisting of parts of Indiana, Armstrong, and Westmoreland counties in which 4 large coal-fired power plants are located. Agreement to participate was obtained from all public elementary schools in the area. Fourteen schools were selected to provide a uniform geographic and age distribution, with all children in Grades 1 through 6 in the schools selected being asked to participate. Testing was completed between February and May 1979.

Questionnaire

The American Thoracic Society, Division of Lung Diseases, 1978 Children's Questionnaire (ATS-DLD-78C) (4), with slight modification, was sent to the homes of all the children. Information was obtained from parents or guardians concerning respiratory symptoms and illnesses in the children, household environmental exposures, and parental smoking history, occupation, and educational attainment. At school, an interviewer-administered cigarette smoking questionnaire was completed away from teachers and other students by each child in Grades 4 through 6. Children were considered cigarette smokers if they had ever smoked 5 or more cigarettes and were currently smoking. Persistent wheeze was defined as wheeze with colds and wheeze occasionally apart from colds, or wheeze on most days or nights.

Pulmonary Function Testing

All pulmonary function tests were administered in the schools by trained technicians using calibrated 8-Liter Stead Wells survey spirometers (Warren Collins, Inc., Braintree, MA). Classroom demonstrations of the forced vital capacity (FVC) maneuver were given, and the students practiced as a group. Standing height was measured in stocking feet. Each child performed FVC maneuvers while seated and without a noseclip. At least 5 attempts were made to obtain a minimum of 3 acceptable FVC maneuvers, using the criteria for acceptability recommended in the ATS statement of the Snowbird Workshop (5).

Acceptable tracings were entered into a computer by hand digitization using a program (6) that rejected tracings with flow continuing at greater than 60 ml/s at the end of expiration. Flow rates at low lung volumes were obtained from smoothed curves by calculating the slopes at given percentages of expired vital capacity. Pulmonary function

SUMMARY Four thousand elementary-school-age children from a rural area of western Pennsylvania participated in a cross-sectional survey that consisted of a standardized respiratory questionnaire completed by their parents and spirometric testing at school. Spirographic tracings were digitized to obtain the FVC, $FEV_{1.75}$, FEF_{25-75}, $Vmax_{75}$, and $Vmax_{50}$, which were standardized for height, age, and sex for the subsequent analyses. Independent associations of potential risk factors with the standardized pulmonary function measures were evaluated with multiple regression techniques. Asthma, persistent wheeze, and parental smoking habits, especially those of the mothers, were associated with lower flow rates. The effect of parental smoking was primarily due to smoking by the mother and was stronger in girls. In female children of currently smoking mothers, FEF_{25-75} was 96% of predicted, $Vmax_{75}$ was 95% of predicted, and $Vmax_{50}$ was 92% of predicted; each flow measure was 98% of predicted in male children of smoking mothers. Prolonged hospitalization at birth was independently associated with lower $FEV_{1.75}$ and flow rates. Low socioeconomic status was associated with lower FVC and $FEV_{1.75}$. Neither current gas stove use nor a history of severe chest illness before 2 yr of age were independently associated with lower levels of pulmonary function. AM REV RESPIR DIS 1984; 130:187-192

measurements from the digitizing program have been shown to be comparable to those made by hand or to direct measures of flow using a pneumotachygraph (6).

Criteria for Test Selection

Testing was considered acceptable if the second largest FVC and forced expiratory volume in one second (FEV_1) were within 10% or 200 ml of the largest values (7). If the subject's tests were acceptable, FVC was selected from the curve with the largest FVC, and forced expiratory volume in three quarters of a second ($FEV_{0.75}$) from the curve with the largest FEV_1. The mean forced expiratory flow rate during the middle half of the FVC (FEF_{25-75}) and the maximal expiratory flows at 75 and 90% of the expired vital capacity ($Vmax_{75}$, $Vmax_{90}$) were the mean values from all curves with an FVC within 10% or 200 ml of the largest FVC. Mean values were chosen to improve the stability of the digitized measures.

Analysis of Data

Pulmonary function measurements were standardized for chest size by regressing the natural logarithm of the measurement on height, age, sex, and product terms of height times age, height times sex, and age times sex. Only those size-standardizing variables that were significant predictors ($p < 0.05$) of the pulmonary function variables were included in models for the subsequent analyses. Even though the logarithmic models explained no more of the variation in pulmonary function measurements than the untransformed models, both normality and homoscedasticity of the residuals (observed minus predicted) were improved by the logarithmic transformations (8). Quintiles of SES derived from parents' occupation and education (3) were grouped into low (V and IV), middle (III), and high (II and I) categories. Black children and children in Grades 4 through 6 who smoked cigarettes were excluded from the analysis.

Potential risk variables were defined categorically (1 = present, 0 = absent), and included persistent wheeze, physician-diagnosed asthma, severe chest illness before 2 yr of age, current cigarette smoking by the mother only, the father only, or by both parents, use of a gas stove for cooking, low SES, and a history of continued hospitalization at birth after the mother was discharged. Crude estimates of the association of these variables with each pulmonary function measure were obtained by adding each variable alone to a multiple regression model, adjusting only for chest size. A stepwise multiple regression was then performed for each pulmonary function measure with the independent variables, including all of the categorically defined variables and the size-standardizing terms. Similar regression models were fit without the respiratory symptom and illness variables. The dose-response relationship between the amount of current parental smoking . . . . . dren's pulmonary function was evaluated by

substituting variables that indicated the number of cigarettes smoked daily (1 to 14, 15 to 24, 25 or more) by each parent for the parental smoking variables. Percents of predicted pulmonary function were generated by transforming the regression coefficients from the log scale to the natural scale.

Modification of the parental smoking associations by either the child's sex or age, or by asthma or persistent wheeze, was tested by introducing interaction (product) terms to the models. For example, the coefficient of an interaction term composed of the product of the child's sex and maternal smoking estimates the differential effect of maternal smoking on girls and boys.

Results

Questionnaires were completed for 4,071 children, 93% of those selected (3). After excluding the 55 black children and the 52 children who smoked, an additional 29 children were excluded because FVC was not acceptably reproducible, 151 because FEV_1 was not reproducible, 275 because neither was reproducible, and 181 because less than 2 acceptable tracings were present. Spirometry was not performed by 153 children who returned questionnaires. The final sample consisted of 3,175 (80.1%) of the 3,964 white, nonsmoking children with completed questionnaires.

Children included in the pulmonary function analysis were compared with children with completed questionnaires who were excluded. No significant differences were present with respect to sex, geographic location, use of gas stoves, parental smoking, SES, or prolonged hospitalization at birth. Prevalences of respiratory symptoms or illnesses were also similar. The mean age of those not included in the analysis ($\overline{X} = 107.8$ months) was significantly lower ($p < 0.01$) than the mean age of those included ($\overline{X} = 114.4$ months), reflecting the ability of older children to perform spirometry better than younger children. Only 69% of children 5 to 7 yr of age had spirome-

try analyzed compared with 87% of those 11 to 14 yr of age (table 1).

Height, age, and sex were significant predictors ($p < 0.05$) of all pulmonary function measures. Boys had lower flow rates (FEF_{25-75}, $Vmax_{75}$, $Vmax_{90}$) but higher FVC and $FEV_{0.75}$ than did girls, after adjusting for height and age. A significant interaction between age and sex was present for all pulmonary function measures, except FVC, with flow rates in girls increasing with age relative to boys. Interaction between age and height was significant only for the flow rates at low lung volumes. No significant interaction between height and sex was present.

After adjusting for the significant size-standardizing terms, each potential predictor was initially evaluated singly without adjusting for the other predictor variables. Variables that were associated with pulmonary function in this crude analysis (table 2) included persistent wheeze, asthma, severe chest illness before 2 yr of age, prolonged hospitalization at birth, SES, parental smoking by only the mother, and smoking by both parents. Gas stove use was significantly predictive only of FVC. Cigarette smoking by only the father was not predictive of any pulmonary function measure.

The associations of each of these variables with pulmonary function in the presence of other significantly predictive variables were evaluated in the stepwise multiple regressions. As in the crude analysis, physician-diagnosed asthma and persistent wheeze were independently associated with lower flow rates (table 3). However, severe chest illness before 2 yr of age was not independently associated with any of the spirometric tests. Only by omitting the variables indicating wheeze and asthma did severe chest illness before 2 yr of age enter the models. A history of a prolonged hospitalization at birth was a significant predictor of lower flow rates and $FEV_{0.75}$.

TABLE 1

AGE DISTRIBUTION OF WHITE, NONSMOKING CHILDREN BY SPIROMETRY STATUS

Age (yr)	Number with Acceptable Spirometry	Number with No or with Unacceptable Spirometry	Total	Proportion with Acceptable Spirometry
5-6	56	22	78	0.72
7	445	199	644	0.69
8	574	142	716	0.80
9	500	133	633	0.79
10	535	132	667	0.80
11	564	89	653	0.86
12	430	57	487	0.88
13-14	71	15	86	0.83
Total	3,175	789	3,964	

. Children of smoking parents had lower flow rates, controlling for all other significant predictors, than did children of nonsmoking parents (table 4). However, FVC was slightly but significantly larger in children of smoking mothers. Exposure to only maternal smoking was associated with reduction in all flow rates, whereas paternal smoking was significantly associated only with lower $Vmax_{90}$. For each pulmonary function measure, the lower function seen in children with both parents smoking was not significantly different from that in children with only a mother smoking. However, the decrease seen in children with only a father smoking was less than that in children with only a mother smoking. Because the association between parental smoking and children's pulmonary function was almost entirely the result of maternal smoking, the subsequent analysis of dose-response and of interaction was limited to maternal smoking.

Decreases in children's pulmonary function associated with maternal smoking did not differ by the amount smoked for any of the pulmonary function measures. A similar lack of dose-response was observed when the analysis was confined to children with nonsmoking fathers. Children of ex-smoking mothers did not have significant differences in pulmonary function from children of nonsmoking mothers.

Testing of the decreases in children's pulmonary function seen with maternal smoking by sex suggested that maternal smoking was associated with lower levels of pulmonary function in female children than in male children; this difference was significant only for $Vmax_{90}$ (table 5). Although levels of pulmonary function in male children of smoking mothers were lower than in children of nonsmoking mothers, the differences were not statistically significant. Similarly, children with persistent wheeze tended to have lower levels associated with maternal smoking than did children without wheeze; however, because of the relatively small numbers of children with both persistent wheeze and a smoking mother, none of the observed differences were significant (table 5). The maternal smoking associations were not significantly changed by the presence of physician-diagnosed asthma, and did not vary according to the child's age.

Low SES was significantly associated with lower FVC and $FEV_{0.75}$, but not with lower flow rates (table 6). Use of a gas stove in the home did not indepen-

TABLE 2

PERCENT OF PREDICTED PULMONARY FUNCTION IN CHILDREN WITH THE POTENTIAL RISK FACTORS: CRUDE ANALYSIS*

	FVC	$FEV_{L.75}$	FEF_{25-75}	$Vmax_{75}$	$Vmax_{90}$
Doctor-diagnosed asthma	102.4[†]	97.2[†]	87.9[‡]	85.0[‡]	87.2[‡]
Persistent wheeze	101.2	97.2[‡]	90.1[‡]	88.7[‡]	91.6[‡]
Chest illness before 2 yr of age	100.4	98.6	95.8[‡]	95.5[†]	95.1[†]
Prolonged newborn hospitalization	100.7	96.5[‡]	91.7[‡]	91.0[‡]	94.6[†]
Only mother smoking	102.1[‡]	100.2	95.8[‡]	94.9[‡]	93.6[‡]
Only father smoking	99.3	99.6	100.3	100.4	100.1
Both parents smoking	100.7	99.6	97.9	97.7	96.6[†]
Gas stove	99.2[†]	99.4	99.7	100.1	99.3
Low SES	98.6[‡]	98.4[‡]	98.4	100.0	101.0

Definition of abbreviations: FVC = forced vital capacity; $FEV_{L.75}$ = forced expiratory volume in 0.75 second; FEF_{25-75} = forced expiratory flow during middle half of FVC; $Vmax_{75}$ and $Vmax_{90}$ = maximal flow after exhalation of 75 and 90% of FVC; SES = socioeconomic status.
* Pulmonary function was standardized for height, age, sex, and their significant ($p < 0.05$) interactions but not for other risk factors. See the text for the definition of each variable. Two-sided p-values test for differences in percent predicted between those children with and those without (100% predicted) the specified characteristic.
[†] $p < 0.05$.
[‡] $p < 0.01$.

TABLE 3

PERCENT OF PREDICTED PULMONARY FUNCTION MEASUREMENTS IN CHILDREN WITH HISTORIES OF SYMPTOMS AND ILLNESSES*

Pulmonary Function Test	Doctor-Diagnosed Asthma (n = 107)	Persistent Wheeze (n = 225)	Chest Illness Before 2 Years of Age (n = 251)	Prolonged Newborn Hospitalization (n = 142)
FVC	102.5[†]	100.6	100.2	99.0
$FEV_{L.75}$	98.7	97.3[‡]	99.4	96.6[‡]
FEF_{25-75}	92.1[‡]	92.6[‡]	99.4	92.6[‡]
$Vmax_{75}$	89.3[‡]	91.9[‡]	99.1	92.0[‡]
$Vmax_{90}$	89.9[‡]	94.6[‡]	97.8	95.7

For definition of abbreviations, see table 2.
* Independent variables were added to models controlling for all other variables that were significant predictors ($p < 0.05$) of the pulmonary function measure. Two-sided p-values test for differences in percent predicted between those children with and those without (100% predicted) the specified characteristic (n = number of children with the specified characteristic).
[†] $p < 0.05$.
[‡] $p < 0.01$.

TABLE 4

PERCENT OF PREDICTED PULMONARY FUNCTION MEASUREMENTS IN CHILDREN WITH PARENTS WHO SMOKE*

Pulmonary Function Test	Only Mother Smokes (n = 268)[†]	Only Father Smokes (n = 689)[†]	Both Parents Smoke (n = 673)
FVC	101.8[‡]	99.5	101.1[‡]
$FEV_{L.75}$	100.1	99.6	99.9
FEF_{25-75}	95.2[§]	98.8	97.6[‡]
$Vmax_{75}$	94.4[§]	99.8	97.4[‡]
$Vmax_{90}$	92.2[§]	96.9[‡]	94.8[§]

For definition of abbreviations, see table 2.
* Independent variables were added to models controlling for all other variables that were significant predictors ($p < 0.05$) of the pulmonary function measure. Two-sided p-values test for differences in percent predicted between those children with and those without (100% predicted) parents who smoke (n = number of children with the specified characteristic).
[†] Includes only subjects with current smoking data on both parents.
[‡] $p < 0.05$.
[§] $p < 0.01$.

TABLE 5

PERCENT OF PREDICTED PULMONARY FUNCTION MEASUREMENTS IN CHILDREN WITH A MOTHER WHO SMOKES, CLASSIFIED BY SEX AND PERSISTENT WHEEZE[*]

		Mother Smoker			
	Mother Nonsmoker (n = 2,066)	Male (n = 536)	Female (n = 523)	Persistent Wheeze (n = 77)	No Persistent Wheeze (n = 982)
FEF_{25-75}	100.0	97.8	95.8[‡]	90.6[†]	97.2[†]
$Vmax_{75}$	100.0	98.0	94.6[‡]	91.7[†]	96.8[†]
$Vmax_{50}$[§]	100.0	97.5	92.1[‡]	92.5	95.0[‡]

For definition of abbreviations, see table 2.
[*] Interaction terms were added to models controlling for all other variables that were significant predictors ($p < 0.05$) of the pulmonary function measures. Two-sided p-values test for differences in percent predicted between children with the specified characteristic and children with nonsmoking mothers (n = number of children with the specified characteristic).
[†] $p < 0.05$.
[‡] $p < 0.01$.
[§] Difference between male and female children of smoking mothers is significant ($p < 0.05$).

dently predict any of the pulmonary function measures.

Discussion

Our findings support the hypothesis that cigarette smoking by parents, especially by the mother, can reduce levels of pulmonary function in their children. The reductions seen with maternal smoking were largely limited to female children and were present only for flow rates. The association persisted after controlling for children's respiratory symptoms and illnesses, and for other variables that might have accounted for the observed association. Other significant independent predictors of the level of children's pulmonary function included prolonged hospitalization at birth, low SES, persistent wheezing, and a diagnosis of asthma. Neither gas stove use nor a history of a severe chest illness before 2 yr of age, after controlling for the other significant predictors, were associated with lower levels of pulmonary function.

Other investigators also have reported an association between parental smoking and children's pulmonary function. Tager and coworkers (9) found an inverse correlation between maternal lifetime cigarette smoking and FEV_1 in male children. These investigators, in another population sample (10), also found that FEF_{25-75} decreased in children of smoking parents as the number of parental smokers increased. More recent findings from this same cohort (11) indicated that maternal, but not paternal, smoking was significantly associated with lower FEF_{25-75} in the children. Yarnell and St. Leger (12), in a small sample of 214 children, found lower $FEV_{0.75}$ and FEF_{25-75} in children whose mothers smoked during pregnancy. Only girls had lower lev-

els of pulmonary function associated with current maternal smoking. Hasselblad and associates (13) reported a dose-response relationship between $FEV_{0.75}$ and current maternal smoking, but found no association with paternal smoking.

Absence of association between parental smoking and children's pulmonary function also has been reported. Leeder and coworkers (14) did not find a significant relationship between peak expiratory flow rate (PEFR) and parental smoking. Schilling and associates (15), in a small population sample of 816 children, examined several pulmonary function measures (FVC, FEV_1, $PEFR$, $Vmax_{50}$, $Vmax_{75}$), and generally failed to find a significant association with maternal smoking; only $Vmax_{50}$ was significantly lower in female children of smoking mothers. This latter finding was interpreted as spurious because there was

TABLE 6

PERCENT OF PREDICTED PULMONARY FUNCTION IN CHILDREN WITH GAS STOVE EXPOSURE AND LOW SOCIOECONOMIC STATUS[*]

Pulmonary Function Test	Gas Stove Exposure (n = 1,631)	Low Socioeconomic Status (n = 1,085)
FVC	99.3	98.6[†]
$FEV_{0.75}$	99.6	98.4[‡]
FEF_{25-75}	100.1	98.4
$Vmax_{75}$	100.2	100.2
$Vmax_{50}$	99.6	101.4

For definition of abbreviations, see table 2.
[*] Independent variables were added to models controlling for all other variables that were significant predictors ($p < 0.05$) of the pulmonary function measure. Two-sided p-values test for differences in percent predicted between those children with and those without (100% predicted) the specified characteristic (n = number of children with the specified characteristic).
[†] $p < 0.05$.
[‡] $p < 0.01$.

no reduction in $Vmax_{75}$ and no reductions were found in male children. However, our data also show that female children of maternal smokers had lower flow rates than did male children. These investigators adjusted for parental pulmonary function before examining the association between parental smoking and children's pulmonary function. Because parental pulmonary function is highly correlated with parental smoking, adjustment for parental pulmonary function may have masked any association of parental smoking with children's pulmonary function. Speizer and coworkers (16), in a large population sample of approximately 8,000 children (the Six-City Study), initially found no association between parental smoking and children's FEV_1. After additional cohorts were added to this sample (1), a small but significant association was found. Dodge (17), in a sample of 676 children, demonstrated no decrease in FEV_1 in children whose parents smoked. As noted, the association in our data between parental smoking and lower levels of children's pulmonary function occurred with those pulmonary function tests that reflect small airway function: FEF_{25-75}, $Vmax_{75}$, and $Vmax_{50}$ (table 4). Failure to demonstrate an association between PEFR or FEV_1 and parental smoking is, therefore, not inconsistent with our findings.

Two reports have presented analyses of the association between parental smoking and FVC; one found no association (15), whereas the other demonstrated a small increase in FVC (1). Our data also show that FVC was slightly but significantly larger in those children exposed to maternal smoking. Chance may be the explanation for this association, although plausible hypotheses can be constructed. An increase in FVC may be due to an increase in the amount of lung parenchyma, to an increase in compliance of the lung or chest wall, or to increased muscularity. Abel and associates (18) found that the lung weight/body weight ratio in female rats whose mothers received nicotine throughout pregnancy was higher than in control animals. No significant differences were observed for other organs. Exposure to nicotine *in utero* may result in an increase in lung parenchyma, which, if subject to normal growth in childhood, might result in an increased vital capacity. Several stimuli in early life have been reported to result in increased lung parenchyma, including hypoxia (19), increased oxygen consumption (20), and human growth hormone

(21). However, the relevance of these stimuli in the setting of passive cigarette smoke exposure is not known.

Because our data are cross-sectional, it was not possible to identify a critical time in a child's life that these effects of parental smoking occur. Limitation of the effect of parental smoking on children's pulmonary function primarily to female children, and finding a small association with paternal smoking but none with ex-smoking, suggested that some effect occurs after birth. Because we have no assurance that ex-smoking mothers smoked during pregnancy, finding no association with ex-smoking does not by itself rule out an effect occurring in utero. The absence of modification of the maternal smoking association by the age of the child in this sample of children 5 to 14 yr of age suggests that the effect either occurs before the age of 5 or is noncumulative. Prospective analyses designed to evaluate the timing of the effect of maternal smoking are needed.

Evidence that the use of a gas stove in the home is associated with lower pulmonary function in children is conflicting and unconvincing. Florey and colleagues (22) demonstrated that NO_2 concentrations in the home were not associated with PEFR, $FEV_{0.75}$, or FEF_{25-75} in children. Keller and coworkers (23) found no decreases in FVC or $FEV_{0.75}$ in subjects from homes with gas stoves. However, only 42% of the eligible sample had pulmonary function measurements, and only half of these were 15 yr of age or younger. Dodge (17) showed no decrease in children's FEV_1 associated with gas stove exposure. Speizer and coworkers (16), in the Six-City Study, and Hasselblad and associates (13) found associations between exposure to a gas stove in the home and lower FEV_1 and $FEV_{0.75}$ in children, respectively, but the latter only in older female children. Subsequent analyses with additional cohorts in the Six-City Study showed associations that, although of similar magnitude, were no longer statistically significant (1).

Ideally, classification of children by parental smoking or gas stove use should pertain to the period in a child's life that the effect is hypothesized to occur. If the effect is due only to current parental smoking or current gas stove exposure, then the classification used here is adequate. However, if the effect of the exposure occurred in the past, then some subjects may have been misclassified. The result of this type of misclassification is

to bias an association toward the null hypothesis of no association (24). Because no association was found between children's pulmonary function and gas stove use, such a bias might be the explanation. However, the association between children's pulmonary function and parental smoking could only have been weakened by a misclassification bias. The failure to find a dose-response relationship between the current level of maternal smoking and children's pulmonary function may have resulted from a similar misclassification. Because data were not collected on the lifetime smoking habits of the parents, it is possible that the current smoking amount did not reflect the dose responsible for the effect. Classification by current smoking category may have blurred the true dosage categories, making the categories similar with respect to true dose.

In the previous analysis of the questionnaire data from our Pennsylvania population (3), a history of severe chest illness before 2 yr of age was associated with a diagnosis of asthma. Thus, failure to find an effect of chest illness on pulmonary function, after controlling for asthma and persistent wheeze, is not surprising. The association between chest illness and asthma could be explained by parents of children with asthma or wheeze preferentially recalling chest illnesses. It is also possible, however, that decrements in pulmonary function associated with chest illness occurred only when asthma or wheeze also were present. In the Tucson population, Burrows and coworkers (25) found an association between respiratory illness before 16 yr of age and airways obstruction in adults. The strength of the association increased with the age of the adult, and was present even after excluding asthmatics. Because our data address only the childhood effects of chest illnesses occurring before 2 yr of age, no direct comparison with the data from the Tucson population is possible.

The observed association between a history of a prolonged hospitalization at birth and lower pulmonary function was unexpected. Infants with bronchopulmonary dysplasia may have lower levels of pulmonary function that persist into childhood (26). Unfortunately, we do not have the data to investigate whether bronchopulmonary dysplasia played a role in the association found in our data.

The independent risk factors identified for diminished pulmonary function in this population of children include pa-

rental cigarette smoking, especially smoking by the mother, prolonged hospitalization at birth, and low SES. Children with asthma or persistent wheeze also had, as would be expected, lower levels of pulmonary function. No independent associations of pulmonary function with gas stove use or severe chest illness before 2 yr of age were found. The long-term effects of these risk factors on pulmonary function are currently unknown and will require prospective evaluation.

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Lebowitz, M.D., Knudson, R.J., Burrows, B. "Family Aggregation of Pulmonary Function Measurements" <u>Am Rev Respir Dis</u> 120: 8-11, 1984.

SUMMARY: Family aggregation of pulmonary function measurements was analyzed in the nuclear families of the Tucson epidemiologic study of airway obstructive diseases (AOD). There were 271 parental pairs and their natural children who had satisfactory pulmonary function data.   Initial regression analysis showed significant correlations of the pulmonary function variables after controlling for age and sex.   Body habitus, as measured by the Ponderal Index, was highly aggregated as well.   Pulmonary function measurements were aggregated in families independent of family size, reported diagnosed AOD, and children's smoking, even though both asthma and smoking showed significant familial aggregation.   After controlling for the familial aggregation of body habitus, a major determinant of pulmonary function, there was no remaining independent aggregation of pulmonary function measurements.   It was also determined that parental passive smoking had no effect on children's pulmonary function measurements.

Family Aggregation of Pulmonary Function Measurements[1-3]

MICHAEL D. LEBOWITZ, R. J. KNUDSON, and B. BURROWS

Introduction

Clinicians have noted that airways obstructive diseases, especially emphysema, appear to run in families, and this has been a common observation since the early nineteenth century (1, 2). Except for the rare homozygotic alpha,-antitrypsin deficiency, other genetic predispositions to chronic obstructive diseases have not been clearly demonstrated (3). Studies in England have demonstrated that there is a genetic basis of asthma (4, 5). Recent studies have demonstrated aggregation of pulmonary function in twins (6, 7), and recent population studies have shown that pulmonary function measurements appear to be aggregated in families (8–10).

It has long been recognized that body size and configuration are genetically determined, yielding familial aggregation of body habitus; body habitus has a major influence on pulmonary function. Although adjustment for height to predict a person's lung function is standard, this is not sufficient when examining interindividual correlations of body habitus with lung function. Thus, it is necessary to evaluate the interaction of body habitus in the analysis of familial aggregation of pulmonary function.

This report attempts to examine the relationship of pulmonary function measurements in the family, of body habitus relationships in the family, and the interaction thereof. The influence of a history of airways obstructive disease in parents and children, smoking in parents and children, family size, and the influence of passive smoking, which are possible confounding variables, are examined as well.

Methods

Data on nuclear families reported herein are derived from the Tucson Epidemiological Studies of Airways Obstructive Diseases, which has been described previously (11). The population under study is a multistage stratified cluster sample of white, non-Mexican-American families in the Tucson area,

SUMMARY Family aggregation of pulmonary function measurements was analyzed in the nuclear families of the Tucson epidemiologic study of airway obstructive diseases (AOD). There were 271 parental pairs and their natural children who had satisfactory pulmonary function data. Initial regression analysis showed significant correlations of the pulmonary function variables after controlling for age and sex. Body habitus, as measured by the Ponderal Index, was highly aggregated as well. Pulmonary function measurements were aggregated in families independent of family size, reported diagnosed AOD, and children's smoking, even though both asthma and smoking showed significant familial aggregation. After controlling for the familial aggregation of body habitus, a major determinant of pulmonary function, there was no remaining independent aggregation of pulmonary function measurements. It was also determined that parental passive smoking had no effect on children's pulmonary function measurements.

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where stratification was on age of head of household and on socioeconomic status.

In the first year of this study (1972–1973), questionnaires were completed on all subjects. These included a respiratory history and a family history with a family tree. Subjects 12 yr of age and older completed their own questionnaires. Mothers, or substitutes if the mothers were not available, completed them for children younger than 12 yr of age (11). Comparisons of maternal and self reporting performed for smoking histories showed no discrepancies. A separate study showed no significant differences, in children 8 to 11, in parental versus self reporting of chronic symptoms (12). Pulmonary function tests were performed satisfactorily in over 90% of those 6 yr of age and older, using techniques previously described (13).

Nuclear families were defined as families in which there were a mother, a father, and at least one natural child of the pair. There were 344 nuclear families of the 1,655 families studied (approximately 25%). The number of subjects involved in these nuclear families represent about 1,400 of the 3,800 subjects in the total study population. There were 271 families in which both parents and 1 or more of their children had satisfactory pulmonary function measurements in the first year of the study. These were analyzed as units. We also considered relationships between parent-child pairs, spouse pairs, and sibling pairs.

The presence of airway obstructive disease in the children and the parent was obtained from the questionnaire, as was smoking history (for those 15 yr of age and older). Family size, obtained from household records, was also used to determine if it was a confounding variable.

As previously described, all measurements were made by trained nurse inter-

viewers; tests of interobserver variability in all measurements indicated no significant differences (11, 13). Standing height (H) in inches, sitting height in inches, and weight (W) in pounds were used to calculate the Ponderal Index (14), an index of body habitus (i.e., $H/\sqrt[3]{W}$). This index had the best correlation with pulmonary function test when compared with other indexes of body habitus.

The pulmonary function measurements used were: forced vital capacity (FVC), forced expiratory volume in one second (FEV$_1$), and maximal expiratory flows after 50 and 75% of the FVC had been expired (Vmax$_{50}$ and Vmax$_{75}$, respectively). Each subject's function was first corrected for height and weight, using regression equations derived from data on asymptomatic nonsmokers in this population. These corrected values did not explain all effects of body habitus.

Comparisons of children's and parent pulmonary function variables (expressed percent predicted) were performed first before accounting for parental body habitus; these were performed before and after Z-score transformations. The Z-scores are standard normal variates: for each subject the observed value was subtracted from t

group mean and divided by the group standard deviation ($z_i = (x_{ijk} - \bar{x}_{jk})/s_{jk}$, for each i subject, j age group, k sex). This removed further effects of age and sex and gave all values the same units. All pulmonary function variables were then adjusted for the individual child's Ponderal Index and the parental Ponderal Indexes (where significantly correlated with the pulmonary function variables) using regression techniques. The Z-scores were recalculated for each of these pulmonary function variables within each age-sex group represented in the parent-child pairs. The Z-score technique is useful for looking at specific effects of other explanatory variables, such as smoking.

Familial aggregation was estimated by analysis of variance (ANOVA), which corresponds to the intraclass correlation as described by Donner and Koval (15). These investigators demonstrated that this method was slightly better than the maximal likelihood estimator if the true correlation was likely to be less than 0.5. Both were better than the usual product-moment correlation method. They also demonstrated that differences in results with inclusion or exclusion of one child were minimal and nonsignificant. The multivariate components of variance method of ANOVA is more useful than other methods of examining aggregation in that it gives separate estimators for variance components and allows usual testing of significance of those estimates. Analyses of variance were performed using the children's pulmonary function measurements as the dependent variable, using age, sex, smoking, and body habitus indexes of the children and the parents as covariates, with parents' pulmonary function (as continuous variables) as the explanatory variables (main effects) in the ANOVA. Covariates were all continuous variables except sex. Main effects were grouped into equal thirds. Two- and three-way interactions were examined. The regression option was used to remove covariate effects, other main effects, and interaction effects from the contribution of each main factor, using SPSS programs on a DEC-10 Cyber 175 University Computer System. In the case of nuclear family analyses using analyses of variance, the analyses were done for all families and separately and for those with 2 or more children (13). For analysis of parent-child pairs, the male/female oldest child was used. For analysis of sibling pairs, the 2 oldest children of each sex in the family were used.

Results

The characteristics of members of the nuclear families with pulmonary function tests are shown in table 1. There were highly significant product-moment correlations of measures of body habitus between all children and their parents, after adjusting for age and sex.

TABLE 1

CHARACTERISTICS OF PARENTS AND CHILDREN
(9 YEARS OF AGE AND OLDER) IN NUCLEAR
FAMILIES WITH PULMONARY FUNCTION

Characteristics	Children (n = 354)		Mothers (n = 276)		Fathers (n = 269)	
	Mean	SD	Mean	SD	Mean	SD
Age	13.5	3.0	38.1	9.8	38.4	12.2
Height (H) (in.)	60.8	7.5	63.9	2.3	68.3	2.5
Weight (W) (lb.)	108.4	41.0	134.8	34.8	172.5	24.8
H/W¹/³	13.1	0.8	12.5	0.7	12.5	0.5
%FVC	110.3	23.9	102.3	16.5	101.2	15.0
%FEV₁	108.5	21.3	104.8	18.9	104.2	17.5
Eversmokers, %	1.7*		50.0		72.3	

Definition of abbreviations: %FVC = percent predicted forced vital capacity; %FEV₁ = percent predicted forced expiratory volume in one second.
* n = 181, 15 yr of age and older only.

The linear regression of all the children's $H/W^{1/3}$ on mothers' $H/W^{1/3}$ had a correlation (r) of 0.804 ($p < 0.0001$); with fathers, r was 0.773 ($p < 0.0001$). There were also some significant product-moment correlations of the amount of smoking (pack-years) between various pairs, especially between fathers and children siblings and spouses ($p < 0.001$), even though many fewer children than parents smoke. The significant correlations were between father and both daughters and sons, between siblings, and between spouses; the mothers-sons correlation of smoking was borderline ($p = 0.085$). There was no correlation of smoking with any of the measurements of body size or habitus.

Product-moment correlations between children's and parents' pulmonary function measurements were statistically significant (r as much as 0.30) prior to adjusting for covariates. The most significant aggregation of a pulmonary function measurement prior to body habitus correction was with FVC, which as a volume measurement is most closely correlated with body habitus. The relationships were also strong and significant for FEV₁, but were less often significant for the flow variables.

However, regressions of the children's percent predicted pulmonary function against parents' pulmonary function and body habitus measurements showed significant correlations of the children's pulmonary function with the parents' body habitus, as well as with their own body habitus. After body habitus and age corrections, the previous correlations of pulmonary function variables between any of the pairs were no longer present. Thus, the relation between children's lung function and parents' lung function is likely to be related to their similar body habitus.

Despite the aggregation of asthma (table 2), it was not a factor in the aggregation of pulmonary function measurements when tested by ANOVA. There was no family aggregation of present diagnosed chronic bronchitis for emphysema. The presence of these other airway obstructive diseases in parents and/or children were not factors in the relationships between pulmonary function measurements in the family (by ANOVA). Family size was not found to be a significant factor in any of the analyses. Analyses of variance for families with 2 or more children only, as well as for all families (1 child or more), yielded similar results.

TABLE 2

PHYSICIAN-CONFIRMED EVER ASTHMA IN NUCLEAR FAMILIES

	No Asthma in Parents	One Parent with Asthma	Both Parents With Asthma
Families, n	273	68	3
Families with 1+ asthmatic child, %	10.8*	28.5	100
Oldest children with asthma, %	8.5	18.1	33.3
Children, n	838	122	11
Children with asthma, %	8.5*	18.7	63.6

* Rates of asthma significantly higher with one or more asthmatic parents ($p < 0.005$).

TABLE 3

CHILDREN'S VOLUME AND FLOW MEASUREMENTS IN RELATION TO PARENTS' VOLUME AND FLOW MEASUREMENTS, CONTROLLING FOR OTHER VARIABLES (BY ANOVA)*

	df†	FVC			$Vmax_{50}$		
		Mean Square	F	p	Mean Square	F	p
No controls							
Father's function	2	3,096.1	8.67	0.001	1,837.5	2.57	0.078
Mother's function	2	2,248.4	4.84	0.009	1,551.8	2.44	0.089
Interaction	4	319.9	0.69	0.600	417.1	0.66	0.624
Explained	8	1,756.2	3.78	0.001	977.4	1.54	0.145
Age, sex, and smoking controls							
Covariate¹	5	4,198.3	10.90	0.001	2,742.5	4.68	0.001
Father's function	2	919.8	2.39	0.094	1,031.3	1.76	0.174
Mother's function	2	1,369.2	3.55	0.030	1,475.8	2.52	0.083
Father's smoking	2	268.8	0.70	0.499	1,366.5	2.33	0.099
Mother's smoking	2	42.9	0.11	0.895	1,128.6	1.93	0.146
2-way interactions¹	24	482.3	1.25	0.199	563.1	0.96	0.519
Explained	37	1,276.2	3.31	0.001	1,052.1	1.80	0.005
Age, sex, and habitus controls,³ adjusted children's function¹							
Covariates¹	4	1,462.8	5.72	0.001	1,631.8	2.55	0.040
Father's function	2	511.4	2.00	0.138	409.1	0.64	0.529
Mother's function	2	274.9	1.08	0.343	88.1	0.14	0.874
2-way interactions	24	487.9	1.91	0.009	944.8	1.48	0.078
3-way interactions	32	382.1	1.49	0.052	420.4	0.66	0.921
Explained	66	623.4	2.44	0.001	770.5	1.21	0.163

Definition of abbreviations: df = degrees of freedom, FVC = forced vital capacity, $Vmax_{50}$ = maximal flow after exhalation of 50% of FVC, F = variance ratio.
"Regression option" (see text).
† Total = 287 without habitus controls, less with habitus data, as complete data missing from 1 or more members of some families.
‡ Parents' habitus also as main effects.
§ No three-way interactions.
‖ Children's function adjusted for their and parents' body habitus (using the Ponderal Index).
¶ All ages, children's sex and smoking/habitus.

To account for all of the possible significant covariables and interactions, we used multivariate analysis of variance to evaluate aggregation of FVC, FEV_1, $Vmax_{50}$, $Vmax_{75}$. Each explanatory variable was treated as an independent contributor to the dependent variable. The results for all 4 pulmonary function variables were similar, so only 1 volume (FVC) and 1 flow ($Vmax_{50}$) variable are shown (table 3).

Without covariate controls or adjusted children's pulmonary function, the parents' volume measurements contributed significantly to the explanation of the children's measurements. These significant relationships for FVC, FEV_1, and $Vmax_{50}$ were also present after age and sex were used as covariates and parental smoking was used as explanatory variables (table 3). However, adjusting for smoking reduced the significance of fathers' FVC and both parents' $Vmax_{50}$. Parents' smoking was significant only for $Vmax_{75}$ (maternal smoking only). Furthermore, we did not find any relation between fathers' or mothers' smoking and their spouses' pulmonary function. The body habitus-corrected FVC and $Vmax_{50}$ of the children as the dependent variables had no significant relationship with any of the explanatory variables, where both the parents' pulmonary function variables had been corrected for body habitus as well. The total amount of variability explained in these analyses was significant for FVC and FEV_1 (p = 0.001).

The analyses of variance performed on the pulmonary function measurements of parent-oldest child, spouse, or sibling pairs yielded negative results.

There were two exceptions to this: the contribution of the father's $Vmax_{50}$ on the daughter's $Vmax_{50}$ was significant (p = 0.046); however, the total variance explained was not significant. As that only left 1 of 24 comparisons significant, mother-son FVC (p of main effect = 0.028), and one might expect approximately 1 of these many comparisons (n = 24) to be significant by chance alone (at p < 0.05), this was considered a chance finding. Performing the same analyses after correcting for smoking habits in the parents and children, and after analyzing by whether airways obstructive diseases were present or not, did not change the results.

The children's Z-score-corrected pulmonary function variables were compared among smoking and nonsmoking parents; the results are shown in table 4. As can be seen, parental smoking did not have a significant effect on children's pulmonary function; smoking habits of others in the household (predominantly siblings) did not have any effect either.

Discussion

It is generally agreed that body habitus is genetically determined; it certainly has high familial aggregation. Pulmonary function variables are measurements that are highly dependent on various characteristics of body habitus. Pulmonary function measurements have previously been shown to aggregate in families when body habitus in the families was not accounted for (8, 9). In our study, we first saw strong correlations between parents' and children's pulmonary function measurements, significant for FVC, FEV_1, and $Vmax_{50}$. However, when we controlled for body habitus in the examination of the relationship between parents' and

TABLE 4

Z VALUES OF CHILDREN'S PULMONARY FUNCTION BY PARENTAL SMOKING

Parental Smoking	n	FVC		FEV_1		$Vmax_{50}$		$Vmax_{75}$	
		Mean	SD	Mean	SD	Mean	SD	Mean	SD
Neither	48	−0.06	1.00	−0.12	0.99	−0.16	1.19	−0.06	1.06
Mother smokes	35	−0.16	0.93	−0.16	0.91	−0.15	0.85	0.0	0.99
Father smokes	92	−0.06	0.91	−0.04	0.97	−0.17	0.95	−0.17	1.01
Both smoke	96	+0.19	1.06	+0.23	1.08	+0.15	0.99	+0.20	0.97
Total	271	0.01	0.99	0.03	1.00	0.0	1.00	0.0	1.00
	df	Mean Square		Mean Square		Mean Square		Mean Square	
Between	3	1.578		2.212		1.386		2.314	
Within	267	0.967		0.975		0.992		0.982	
F		1.632		2.268		1.398		2.358	
p		0.182		0.081		0.244		0.072	

For definition of abbreviations, see table 3.

children's pulmonary function measurements, we no longer found such relationships. Thus, familial correlations for observed pulmonary function, especially FVC, were dependent on familial aggregation of body habitus, even after controlling for age and sex. It can not be construed as an overadjustment of familial data, as the underlying familial aggregation is one of body habitus characteristics. This is more a genetic effect than one of dietary or environmental effect, as shown by the weaker relationship between siblings and the lack of a relationship of body habitus between spouses.

On the other hand, we did detect a familial relationship of asthma between children and parents independent of smoking and pulmonary function measures (table 2), which confirmed findings of Sibbald and coworkers (4, 5), and Townley and associates (16). To insure that this is not strictly a result of reporting bias, objective measures such as bronchial-reactivity would have to be done to confirm the relationship, as has been done by Townley and associates (16). This familial aggregation of asthma did not affect the findings for any familial aggregation of pulmonary function.

We found also that smoking habitus aggregated in families but was probably an environmental influence only. Spouses and siblings had the closest relationships of smoking habits ($r = 0.29$ and 0.50, respectively). Smoking habits of both sons and daughters correlated more highly with those of their fathers ($r = 0.22$ and 0.23, respectively) than with those of their mothers ($r = 0.08$ and 0.03, respectively).

Previously, we had not found a relationship between children's and parents' chronic symptoms by parental smoking (20). When we examined effects of parental smoking on children's pulmonary function, taking into account the interrelationship between parents' and children's pulmonary function, only maternal smoking was a significant explanatory variable, and

only for $V_{max_{75}}$ ($p = 0.043$). Considering the number of ways in which the comparisons were made, this one difference probably was not meaningful. When children's pulmonary function was adjusted for paternal body habitus as well as their own, there was no significant parental smoking contribution. A lack of a relationship between parental smoking and children's pulmonary function, even without correcting for parental pulmonary function or body habitus, had been reported by Speizer and coworkers (17, 18), Schilling and associates (10), and Dodge (12). Tager and colleagues (19) had reported this association, but it too might disappear if corrected for the family aggregation they found (9), and/or body habitus. It is possible that controlling for body habitus in a family may be controlling for other genetic and host factors as well.

Finally, we did not find any significant interaction between the smoking habits of either parent smoking and their spouses' lung function (table 3), similar to Comstock and coworkers (21) and Schilling and associates (10), but different from Kauffmann and coworkers (22).

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Health of Children: A Cross-sectional Study" <u>Pediatr Pulmonol</u> 1:
262-266, 1985.

SUMMARY: To investigate the effects of air pollution on the
respiratory health of children, a subject of some controversy, a
comparative study was undertaken of 2,385 school children who lived
in central urban, peripheral urban, and suburban areas. Daily
monitoring of sulphur dioxide and total suspended particle
concentrations in all areas showed that pollutant concentrations
in central and peripheral urban areas were above commonly accepted
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any acute respiratory symptoms. Children also performed standard
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suburban area. These differences persisted after corrections for
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cough in children. Although boys had higher lung volumes and lower
air flow, regression analysis showed no significant influence of
the interactions "sex-geographic area" and "sex-smoking" on lung
function. It was concluded that air pollution had a significant
effect on the respiratory health of children.

The Effects of Air Pollution on the Respiratory Health of Children:
A Cross-sectional Study

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Summary. To investigate the effects of air pollution on the respiratory health of children, a subject of some controversy, a comparative study was undertaken of 2,385 school children who lived in central urban, peripheral urban, and suburban areas. Daily monitoring of sulphur dioxide and total suspended particle concentrations in all areas showed that pollutant concentrations in central and peripheral urban areas were above commonly accepted safety levels for respiratory health, while concentrations in the suburban area were within acceptable limits. A questionnaire administered to each mother assessed environmental exposure to pollutants in the household, the occurrence of respiratory symptoms as well as lung diseases as diagnosed by a physician, and general information. Children were interviewed about smoking habits and any acute respiratory symptoms. Children also performed standard lung function tests. Results showed that children from both urban areas had lessened pulmonary function and a higher prevalence of bronchial secretion with common colds than did those from the suburban area. These differences persisted after corrections for exposure to indoor pollutants, active or passive smoking, socieconomic status, and sex. Parental cigarette smoking was related to a fall in forced, expiratory volume in 1 second and an increased incidence of acute respiratory illnesses and chronic cough in children. Although boys had higher lung volumes and lower air flow, regression analysis showed no significant influence of the interactions "sex-geographic area" and "sex-smoking" on lung function. It was concluded that air pollution has a significant effect on the respiratory health of children. (Key words: active and passive smoking; respiratory health of children; sulphur dioxide; total suspended particle conc.; urban vs suburban air pollution.) *Pediatr Pulmonol 1985; 1:262-266.*

Although many authors have reported that air pollution has a negative effect on the respiratory health of children,[1-6] this finding has not been confirmed by others.[7-9] According to Ericsson and Camner[10] these contrasting results could be due either to the different degree of exposure of the tested populations or to the inadequate assessment of exposure when data collected from one or two monitoring stations are considered to be representative for the whole area.

The purpose of the present study was to compare the respiratory health of children from two urban areas with that of a control group from a suburban, semirural area. All subjects lived within 500 meters from a monitoring station.

Methods

The study was undertaken during the winter of 1980–1981 in two urban areas of Turin, one central (UC) and one peripheral (UP), and in a suburban area (SU) that served as a control.

Seven stations scattered throughout each of the three areas monitored daily sulphur dioxide (SO_2) and total suspended particle (TSP) concentrations. SO_2 was measured using a coulometric analyzer (PW 9,700 Philips, Philips Electronic Instruments Inc., Mahwah, N.J.) and TSP by a gravimetric method (Gelman low rate sequential sampler, Gelman Sciences, Inc., Ann Arbor, Mich.).

To ensure as far as was possible that the population had been uniformly exposed to air pollutants, we recruited, in each of our three geographic locations, children living in the same area who were attending the sixth grade at a junior high school located within 500 meters from a monitoring station.

Respiratory health was assessed by means of lung function measurements and a question-

naire. The questionnaire, administered to mothers, supplied information about general data, environmental exposures to pollutants in the household, respiratory symptoms, lung diseases diagnosed by a physician, and parental history; the latter included questions about education, occupation, smoking habits, and respiratory health. Each child was interviewed confidentially about his or her smoking habits and any acute respiratory symptoms.

Flow-volume curves were obtained by means of a Hewlett-Packard 40801 M computerized pneumotachograph (Hewlett-Packard Company, Waltham, Mass.). The best forced vital capacity (FVC), forced expiratory volume in 1 second (FEV_1), forced expiratory flow between 25 and 75% of FVC (FEF_{25-75}), and maximal expiratory flow at 50% of FVC ($\dot{V}max_{50\%}$) were selected according to Taussig et al.[11] Lung function tests were not performed until ten days following recovery in subjects with acute respiratory illness.

General linear model analysis (GLM) was done taking lung function values as dependent variables.[12] The set of independent variables included: geographic area; sex (male = 1, female = 0); age; height; body weight; active and passive smoking (yes = 1, no = 0, and daily number of cigarettes); socioeconomic status defined as father's total years of education; central heating (yes = 1, no = 0); type of stove (gas = 1, electric = 0); and exhaust hood (unused = 1, used = 0). Geographic areas were compared using Sheffe's method.[13]

To evaluate the effect of air pollution on respiratory symptoms and diseases a logistic regression analysis[14] was performed using geographic area, sex, active and passive smoking, socioeconomic status, central heating, stove type, and exhaust hood use as independent variables. The interactive effect of independent variables as they related to dependent variables (lung function; respiratory symptoms and illnesses) were evaluated, and the usual criteria for significance were used.

Results

The mean concentrations of pollutants for the winter months (October to April) as well as for the year in the three areas are shown in Figure 1. Out of 2,439 eligible children, 2,385 (1,266 boys and 1,119 girls) entered the study. The remaining 54 subjects were not included because
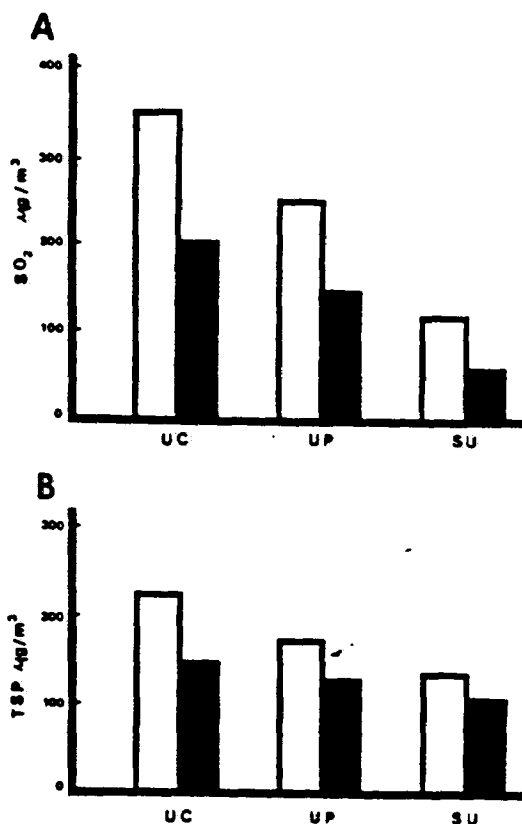

figure 1—Concentrations of (top) Sulphur dioxide (SO_2) and (bottom) total suspended particles (TSP) in central (UC), peripheral (UP) and suburban (SU) areas during the winter (October to April) of 1980–1981 (white bars) and for the whole year (dotted bars).

of parental objections (14 cases) and other reasons.

General data (Table 1) indicated that the number of boys was greater, although not significantly so, in UP, while the socioeconomic status was significantly higher in SU. As the prevalence of current smokers was very low (1.3%), children who had smoked even one cigarette during their lifetime were considered to be smokers; a significantly higher prevalence of smoking was found in UC ($P < 0.01$).

The adjusted prevalence rates of respiratory symptoms and illness computed from logistic multiple regression (table 2) showed that the rate of bronchial secretions with common colds was significantly higher in urban areas, while that of asthma was significantly lower. Although some symptoms and diseases were less common among girls, we did not observe any interaction

table 1—Characteristics of the Study Population by Geographic Area and Sex in Absolute Numbers, Nearest Percentage or Mean (SD)

	Boys			Girls		
-	UC	UP	SU	UC	UP	SU
No. of subjects	359	813	94	360	668	91
Age (years)	11.2 (0.4)	11.3 (0.4)	11.1 (0.4)	11.1 (0.4)	11.3 (0.4)	11.2 (0.4)
Height (cm)	148 (7.0)	149 (7.0)	149 (7.0)	146 (7.0)	147 (7.0)	147 (7.0)
FTE (years)	6.1 (3.0)	6.2 (3.5)	6.8 (3.2)	6.1 (2.8)	6.3 (3.6)	6.9 (3.2)
Smoking habit (%)						
Father	60	62	54	65	62	59
Mother	23	23	25	23	24	21
Child*	15	7	4	9	5	3
Exhaust hood (%)	28	21	43	30	20	46
Gas stove (%)	99	99	99	99	99	99
Central heating (%)	30	29	32	31	29	31

Key:
UC = urban central.
UP = urban peripheral.
SU = suburban.
FTE = father's total years of education.
* The prevalence of smoking in UC vs other areas is significant (P < 0.01).

of the variable sex–geographic area and respiratory illness. The number of cigarettes smoked by both father and mother (UC) had a significant interaction on the rate of cough with cold (P < 0.01) and acute respiratory illness (P < 0.01). There was a strong correlation between active smoking and a significant increase in the rate of chronic cough (P < 0.01), but this symptom had such a low prevalence that the finding must be regarded with caution.

We detected, in both sexes, a significant association between geographic area and lung function (Table 3), with a lower FEV$_1$ and forced airflow rates being observed in both urban areas. Notwithstanding the difference between sexes, the interaction sex–geographic area produced no further effect on lung function.

The FEV$_1$ was significantly decreased by passive smoking (P < 0.01), while FEF$_{25}$ and V$_{max}$ were affected negatively by active smoking (P < 0.01). Active smoking by mother or father, the use of a gas stove and exhaust hood, and all the other interactions had no statistically significant effect on lung function.

Discussion

The significantly lower FEV$_1$ and airflow rates and the higher prevalence of bronchial secretion during acute respiratory infections found in children from the two urban areas suggest that a consistent level of air pollution has a negative effect on respiratory health. In both urban areas the annual average concentrations of SO$_2$ and particulates were well above 100 μg/m^3, a level that, according to the World Health Organization,[14] can cause adverse effects.

The results of this study are in agreement with those reported by Saric[2] and Chapman in a population exposed to similar levels of air pollutants. Although other authors have not found that exposure to air pollution has any significant effect on respiratory health, this discrepancy is probably due to in one instance to an insufficient sample size[9] and in another to the negligible pollution concentrations.[8] The results of a study that had both an adequate sample size and levels of pollution (Kerrebijn[7]) could have been affected by the selection of a geographic area as a control that had been cleaned only one year before the study.

In accord with the findings of Rasmussen et al. in adults,[17] we found higher expiratory flows in children living in houses with central heating. Indoor air pollution, expressed as the presence of gas stoves and unused exhaust hoods, had no significant effect on respiratory health, confirming the results of Melia.[18]

Both active and passive smoking had a negative effect on respiratory health. Passive smoking only had an adverse effect when both parents smoked; no association was found between children's respiratory health and maternal smoking. This finding is at variance with other reports[19,20] and can be explained by the low ex-

posure of our population to maternal smoking because of the small numbers of mothers who smoked and the high numbers who worked outside the home (40%).

Although, as has been reported previously,[21-23] boys from the three areas had 1) a higher prevalence of wheezing, shortness of breath, and asthma; 2) lower airflow rates; and 3) higher lung volumes, no significant influence of the interaction sex-geographic area on lung function or respiratory illness was detected. In contrast with other studies[19,24,25] we did not observe that boys

table 2—Prevalence (%) of Respiratory Illness and Symptoms Adjusted for Socioeconomic Status and Active and Passive Smoking in the Three Geographic Areas

	Geographic Areas				
	UC	UP	SU	Effects	p
Cough with colds					
Boys	48.1	48.0	48.2	Area	NS
				Sex	NS
Girls	42.0	43.1	41.2	Sex, Area	NS
Chronic cough					
Boys	0.6	0.5	0.4	Area	NS
				Sex	NS
Girls	0.7	0.6	0.5	Sex, Area	NS
Bronchial secr.					
Boys	23.8	22.2	15.1	Area	<0.01
				Sex	NS
Girls	21.8	21.1	15.0	Sex, Area	NS
Chronic bronchial secr.					
Boys	0.8	0.8	0.6	Area	NS
				Sex	NS
Girls	0.9	0.8	0.6	Sex, Area	NS
Wheezing					
Boys	5.5	5.5	5.3	Area	NS
				Sex	<0.01
Girls	2.1	2.1	2.0	Sex, Area	NS
Shortness of breath					
Boys	3.0	3.1	3.9	Area	NS
				Sex	<0.01
Girls	1.5	1.8	1.6	Sex, Area	NS
Asthma					
Boys	1.6	1.8	4.3	Area	<0.01
				Sex	<0.01
Girls	0.7	0.8	1.1	Sex, Area	NS
ARI					
Boys	20.1	20.5	21.0	Area	NS
				Sex	NS
Girls	19.2	19.8	21.0	Sex, Area	NS
RT(2)					
Boys	16.0	15.5	16.1	Area	NS
				Sex	NS
Girls	15.9	16.0	16.2	Sex, Area	NS

Key:
UC = urban central.
UP = urban peripheral.
SU = suburban.
ARI = acute respiratory illness in the last two years.
RT(2) = respiratory troubles in the first two years of life.

table 3—Means of Lung Function Measures Adjusted for Age, Height, Socioeconomic Status, Active and Passive Smoking, and Central Heating in the Three Geographic Areas

	Geographic Areas				
	UC	UP	SU	Effects	p
FVC (l)					
Boys	2.77 a	2.76 a	2.81 a	Area	NS
				Sex	<0.001
Girls	2.57 b	2.59 b	2.57 b	Sex, Area	NS
FEV₁ (l)					
Boys	2.36 a	2.36 a	2.42 b	Area	<0.001
				Sex	<0.001
Girls	2.27 c	2.31 c	2.34 d	Sex, Area	NS
FEF₂₅₋₇₅% (l/s)					
Boys	2.76 a	2.82 a	2.91 b	Area	<0.001
				Sex	<0.001
Girls	2.98 c	3.04 c	3.13 d	Sex, Area	NS
V̇ₘₐₓ₅₀ (l/s)					
Boys	3.28 a	3.30 a	3.41 b	Area	<0.020
				Sex	<0.001
Girls	3.50 c	3.52 c	3.66 d	Sex, Area	NS

Key:
UC = urban central.
UP = urban peripheral.
SU = suburban.
a, b, c, and d indicate differences among areas (identical letters mean no significant difference).

had a different sensitivity to passive or active smoking than did girls. In our population, sex did not modify the response to air pollution and smoking.

The greater number of asthmatics in the SU group was independent of socioeconomic status and might be due to a higher allergen concentration in this semirural area. This hypothesis needs to be confirmed by pollen monitoring and allergologic studies.

We conclude that air pollution, active smoking, and passive smoking when both parents smoke have a negative effect on the respiratory health of children.

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ABSTRACT. Results are reported from a study of the association between exposure to sidestream cigarette smoke or gas stove emissions and pulmonary function level and growth rate of 7,834 children seen at 2-5 annual visits between the ages of 6-10 years. Children whose mothers smoked one pack of cigarettes per day had levels of forced expiratory volume in one second (FEV1) at age eight that were 0.81% lower than children of nonsmoking mothers (p<0.0001), and FEV1 growth rates approximately 0.17% per year lower (p = 0.05). For a child of age eight with an FEV1 of 1.62 liters, this corresponds to a deficit in rate of change of FEV1 of approximately 3 ml/annum and a deficit of 13 ml at age eight. Children whose mothers smoked one pack per day had levels of forced vital capacity (FVC) at age eight that were 0.33% higher than children of nonsmokers (p = 0.12); however, their growth rates of FVC were 0.17% per year lower (p = 0.04). Because few mothers changed their smoking habits during the course of the study, it was not possible to determine whether the difference in rate of growth was due to current exposure or to an effect of prenatal and early childhood exposure on the course of development. The magnitude of the effect on FEV1 is consistent with deficits in FEV1 of up to 3% in early adult life due to childhood exposure to sidestream cigarette smoke. The importance of this relatively small effect will be evaluated further through follow-up of these children as they are exposed to other risk factors such as personal active smoking. The data provide some evidence for an association between gas stove exposure and pulmonary function level, especially at younger ages, but no evidence for an effect of gas stove exposure on growth rate.

INDOOR AIR POLLUTION AND PULMONARY FUNCTION GROWTH IN PREADOLESCENT CHILDREN

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Berkey, C. S., J. H. Ware, D. W. Dockery, B. G. Ferris, Jr. (Harvard School of Public Health, Boston, MA 02115), and F. E. Speizer. Indoor air pollution and pulmonary function growth in preadolescent children. *Am J Epidemiol* 1986;123:250–60.

Results are reported from a study of the association between exposure to sidestream cigarette smoke or gas stove emissions and pulmonary function level and growth rate of 7,834 children seen at 2–5 annual visits between the ages of 6–10 years. Children whose mothers smoked one pack of cigarettes per day had levels of forced expiratory volume in one second (FEV_1) at age eight that were 0.81% lower than children of nonsmoking mothers ($p < 0.0001$), and FEV_1 growth rates approximately 0.17% per year lower ($p = 0.05$). For a child of age eight with an FEV_1 of 1.62 liters, this corresponds to a deficit in rate of change of FEV_1 of approximately 3 ml/annum and a deficit of 13 ml at age eight. Children whose mothers smoked one pack per day had levels of forced vital capacity (FVC) at age eight that were 0.33% higher than children of nonsmokers ($p = 0.12$); however, their growth rates of FVC were 0.17% per year lower ($p = 0.04$). Because few mothers changed their smoking habits during the course of the study, it was not possible to determine whether the difference in rate of growth was due to current exposure or to an effect of prenatal and early childhood exposure on the course of development. The magnitude of the effect on FEV_1 is consistent with deficits in FEV_1 of up to 3% in early adult life due to childhood exposure to sidestream cigarette smoke. The importance of this relatively small effect will be evaluated further through follow-up of these children as they are exposed to other risk factors such as personal active smoking. The data provide some evidence for an association between gas stove exposure and pulmonary function level, especially at younger ages, but no evidence for an effect of gas stove exposure on growth rate.

forced expiratory volume; forced vital capacity; longitudinal studies; nitrogen dioxide; smoking, passive; tobacco smoke pollution

Although outdoor air pollution has long been recognized as a potential health hazard, the contaminants of indoor air from either the passive diffusion of outdoor air to the indoors or from indoor sources have only recently received similar attention. A recent National Academy of Science report (1) concluded that the principal population exposure to several pollutants may be associated with activities inside the home. In particular, "for many people the main or sole exposure to numerous gaseous and particulate compounds results from passive exposure to tobacco smoke," (1, page V-2) and "unvented gas cooking is probably responsible for a large portion of nitrogen dioxide exposures in our population" (1, page ES-8).

Several epidemiologic studies have reported higher frequencies of respiratory illnesses or reduced pulmonary function levels among children exposed to sidestream cigarette smoke (2-7). Although some investigators have not found such associations (8-11), the bulk of the evidence strongly supports a positive relationship. The evidence regarding the health effects of gas stove emissions has been less consistent. Melia and coworkers (12, 13) reported increased illness and symptom rates but no reduction in pulmonary function level among children exposed to gas stove emissions, while Speizer and colleagues (7, 14) found lower pulmonary function levels but no increases in illness or symptom frequencies. Keller et al. (15) reported no associations and Hasselblad et al. (4) found reduced pulmonary function levels only among older girls.

Since each of these studies relied on cross-sectional data, little is known about the association between exposure to indoor air pollutants and growth rate of pulmonary function. A recent report, however, has suggested that pulmonary function growth rates may be affected by exposure to sidestream cigarette smoke (16). The Harvard Study of Air Pollution and Health, an ongoing longitudinal investigation of the health effects of air pollutants, both indoor and outdoor, provides an opportunity for further investigation of this question. This report describes the association between the rates of change of two measures of pulmonary function—forced expiratory volume in one second and forced vital capacity—and exposure to sidestream cigarette smoke or gas stove emissions among a sample of 7,834 children receiving spirometric examinations on two or more occasions between their sixth and tenth birthdays. Estimated pulmonary function levels at eight years of age are also investigated for associations with pollutant exposure.

MATERIALS AND METHODS

The study enrolled 12,252 children in six geographic areas of the eastern and midwestern United States (Watertown, MA; Kingston and Harriman, TN; Steubenville and Mingo Junction, OH; a geographically defined section of St. Louis, MO; Portage, WI, and several surrounding communities; and Topeka, KS) between 1974 and 1981. At the initial and subsequent annual examinations, children were seen in their schools for determination of height and weight and for a spirometric examination. At each visit, children took home a standardized questionnaire to be completed by a parent or guardian. The questionnaire requested information about parental smoking habits, type of cooking fuel used in the home, parental education, and respiratory illness and symptom histories for the participating child and the parents. Each child in grade four or higher was asked privately about personal smoking habits. Additional information regarding the study design is provided elsewhere (17).

Standing height and weight were measured in stocking feet and the children performed forced expiratory maneuvers on a water-filled recording spirometer (Survey Spirometer, Warren E. Collins, Braintree, MA) while sitting with free mobility and without a noseclip. Each child performed at least five forced expirations but not more than eight. Forced vital capacity (FVC) and forced expiratory volume in one second (FEV₁) were measured for each blow judged acceptable by the examiner. The mean of

the best three efforts was calculated after correction for body temperature and water saturation. A more detailed description of the measurement procedures is given elsewhere (18).

The analyses presented were restricted to white children with at least two acceptable pulmonary function measurements between their sixth and tenth birthdays. We excluded five-year-olds because of the poorer cooperation and greater learning effect seen in this age group (18). The tenth birthday was selected as the upper limit to avoid the adolescent growth spurt for most children. Dickman et al. (19) found that the pulmonary function growth spurt begins when the child is about 154 cm tall, which fewer than 3 per cent of children reach by age 10 (20). Detels et al. (21) found that peak growth velocity for FEV_1 occurred about one year after peak growth velocity for height, which occurred at age 10 for girls and at age 12 for boys.

For this report, an examination was excluded if the child reported smoking at least one cigarette per week at the time of the examination. The data for each child were reviewed longitudinally, as described in the next section, to identify atypical values.

Statistical methods

For each spirometric examination, we produced a predicted FEV_1 and FVC based on the child's height, weight, sex, and age. Previous work had shown that analyses of children's pulmonary function measurements should utilize the natural logarithmic transformation (18). For this analysis, predicted values for the logarithms of FEV_1 and FVC were calculated using the model developed in that work, but with regression coefficients re-estimated from the data set analyzed for this report. The model included the logarithms of height, weight, and age plus an indicator variable for sex and a sex-specific height term. An FEV_1 residual, defined as the difference between the logarithms of the observed and predicted FEV_1 values, was then calculated for each examination. An FVC residual was calculated similarly.

To identify children with inconsistent observations, standard deviations of these FEV_1 residuals, and separately of the FVC residuals, were computed for each child. Sixty-six children had strikingly large standard deviations for either FEV_1 or FVC (more than 5 standard deviations from the sample mean). The serial values for each of these children were reviewed. In each instance, a clearly erroneous value was found and the FEV_1 and FVC for that examination were deleted from that child's record.

Analysis of the FEV_1 or FVC residuals was based on a two-step growth curve method (22). In the first step of the analysis, each child's series of pulmonary function residuals was regressed on the ages (centered at eight years) at the successive examinations. The coefficients of the fitted regression line provided estimates of the child's pulmonary function *growth rate* and *level* at age eight. The antilogarithm of this growth rate times 100 expresses each child's rate of change of pulmonary function as a percentage of the population mean annual growth rate. The antilogarithm of the level times 100 is the child's per cent of predicted pulmonary function at age eight. The expression of pulmonary function level at an age common to all children was required for comparability in subsequent analysis of risk factors. For clarity, we report the level and growth rate as differences from 100 per cent. Thus a child whose observed pulmonary function values were all equal to the predicted values would have a level of 0 per cent and growth rate of 0 per cent per year.

Figure 1 illustrates this method of summarizing the FEV_1 values for an individual child, a girl who had four examinations. Her logarithm (FEV_1) values are plotted against the four ages; also shown are the predicted logarithm (FEV_1) values. The differences between each pair of points are the four FEV_1 residuals. The regression line fitted to these four residuals yields the estimated FEV_1 growth rate and level for this child.

The second step of the growth curve method used the coefficients of these fitted
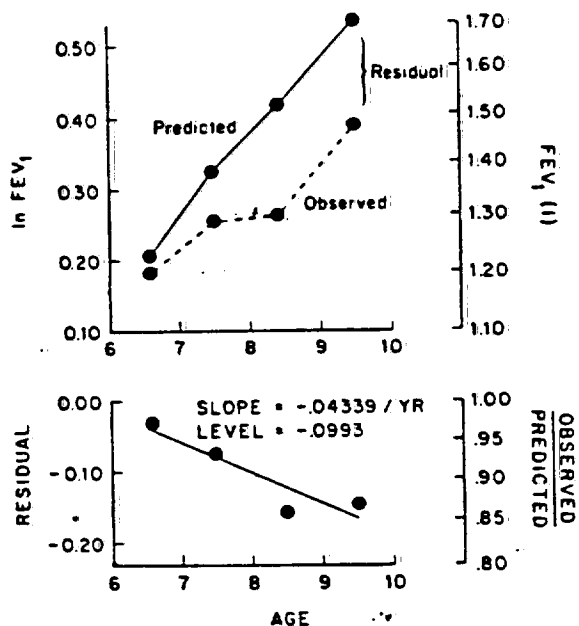
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FIGURE 1. Calculation of growth rate and level of ln(FEV$_1$) for an individual child. The residuals in the upper panel, i.e., the difference between observed and predicted ln(FEV$_1$), were regressed on age in the lower panel.

regression lines as the dependent variables in a further regression analysis. Specifically, the estimated levels and growth rates for FEV$_1$ and FVC (thus, four dependent variables) were analyzed separately by weighted least squares regression. Each weighting variable was the inverse of the estimated variance of the individual level or slope, defined as the sum of the between-subject and within-subject variances. The between-subject variance was common to all children, but the within-subject variance, and therefore the weight, depended on the number of examinations and the ages at examination. In particular, children with only two observations received the lowest weights. The variance components were estimated by an iterative procedure based on the methodology of Hui and Berger (23) and Fay and Herriot (24). These weights also were used to calculate weighted means of FEV$_1$ and FVC level and growth rate for the full sample and for subgroups defined by values of demographic variables and risk factors. All

weighted means and regression coefficients were exponentiated and expressed in per cent.

The independent variables of primary interest included parental smoking habits and type of cooking stove. Maternal and paternal smoking status was defined by classifying each parent as a smoker if they were reported to be a current smoker at any examination and a nonsmoker otherwise. Maternal and paternal smoking level was defined as the average over examinations of number of cigarettes smoked per day. Stove type was defined as the proportion of examinations with a positive response for gas stove.

Four different models for effects of parental smoking were considered (table 4). Model 1 included both maternal and paternal smoking status, Model 2 included only maternal smoking status, and Model 3 included the number of parents who smoked. Model 4 included maternal smoking level to investigate the existence of an exposure-response relationship. Each analysis also

included indicator variables identifying the geographic area of residence and a three-level variable for socioeconomic status based on the average number of years of education of the child's parents (less than nine, nine to 12, more than 12). Other variables considered in the analysis included a reported history (yes/no) of physician-diagnosed respiratory illness before two years of age and a history (yes/no) of bronchitis prior to the initial examination.

RESULTS

Sample

Between the 1974–1975 and 1980–1981 school years, 12,252 children less than 10 years of age were seen at least once. Of these, 11,140 were white and 1,112 were from other racial groups. This analysis is restricted to the 7,867 white children who had at least two acceptable pulmonary function examinations during that period. Fourteen measurements were eliminated because the child reported smoking at least one cigarette per week at the time of the examination. Ninety-nine additional measurements were excluded because they were inconsistent with the other serial measurements from the same child; this included the complete elimination of 33 children with two inconsistent observations. The remaining 22,901 observations from 7,834 children represented 88.4 per cent of all observations collected for white children between six and 10 years of age. When examinations are grouped by half-years of age, the mean values of the unadjusted FEV_1, height, and weight are slightly higher for boys than for girls (table 1).

Demographic variables and respiratory health

The mean (deviation from predicted) FEV_1 level at eight years of age for the 7,834 children was −0.02 per cent (table 2) and the mean (deviation from predicted) growth rate was +0.03 per cent per year. Neither of these values differed significantly from 0. Mean FVC level was −0.13 per cent and mean growth rate was +0.15 per cent per year. The growth rate for FVC was significantly different from 0 ($p < 0.01$). Mean values for boys and girls were not significantly different for any measure (table 2).

Earlier reports from this study (18) in-

TABLE 1

Mean FEV_1, FVC, height, and weight by age and sex for 7,834 children examined 2–5 times between their 6th and 10th birthdays

Age group (years)	No.	FEV_1 (liters)	FVC	Height (meters)	Weight (kg)
		Boys			
6–	456	1.294	1.471	1.181	22.75
6.5–	982	1.356	1.544	1.204	24.05
7–	1,341	1.440	1.656	1.236	25.38
7.5–	1,655	1.519	1.749	1.260	26.67
8–	1,865	1.617	1.873	1.291	28.40
8.5–	1,849	1.692	1.969	1.318	30.10
9–	1,739	1.787	2.083	1.346	31.80
9.5–<10	1,660	1.866	2.181	1.373	33.82
		Girls			
6–	480	1.210	1.352	1.174	22.14
6.5–	1,002	1.276	1.429	1.197	23.43
7–	1,299	1.373	1.539	1.229	25.06
7.5–	1,700	1.425	1.605	1.253	26.29
8–	1,745	1.519	1.714	1.285	28.15
8.5–	1,827	1.593	1.807	1.311	29.71
9–	1,689	1.690	1.917	1.341	31.73
9.5–<10	1,612	1.768	2.010	1.369	33.63

TABLE 2

Weighted means (standard errors) of pulmonary function levels and growth rates (deviations from predicted) of 7,834 children, by sex, number of examinations, city of residence, parental education, and illness history

Variable	No.	FEV_1 Level (%)	FEV_1 Growth rate (%/year)	FVC Level (%)	FVC Growth rate (%/year)
Total	7,834	−0.02 (0.12)	+0.03 (0.05)	−0.13 (0.12)	+0.15 (0.05)
Sex					
Boys	3,989	−0.03 (0.27)	+0.03 (0.07)	−0.04 (0.17)	+0.14 (0.07)
Girls	3,845	−0.08 (0.17)	+0.03 (0.07)	−0.21 (0.17)	+0.17 (0.07)
No. of examinations					
2	2,571	−0.53 (0.24)	+0.34 (0.14)	−0.72 (0.22)	+0.84 (0.12)
3	3,099	+0.26 (0.19)	+0.10 (0.08)	+0.09 (0.18)	+0.24 (0.07)
4	2,040	+0.05 (0.22)	−0.11 (0.07)	+0.16 (0.22)	−0.18 (0.07)
5	18	−2.15 (2.34)	−0.09 (0.66)	−1.17 (2.33)	−1.00 (0.71)
3+	5,157	+0.17 (0.14)	+0.02 (0.06)	+0.11 (0.14)	+0.07 (0.05)
City					
Portage, WI	1,250	+1.92 (0.31)	−0.41 (0.12)	+2.19 (0.30)	−0.61 (0.12)
Topeka, KS	1,216	−0.97 (0.32)	+1.06 (0.14)	−1.06 (0.31)	+1.71 (0.13)
Watertown, MA	1,334	−1.06 (0.29)	+0.15 (0.11)	−2.25 (0.28)	+0.18 (0.11)
Kingston, TN	993	−0.64 (0.35)	−0.25 (0.14)	+0.11 (0.34)	−0.26 (0.14)
St. Louis, MO	1,546	−0.07 (0.28)	−0.01 (0.11)	−0.19 (0.27)	+0.23 (0.11)
Steubenville, OH	1,495	+0.50 (0.28)	−0.19 (0.11)	+0.51 (0.27)	−0.08 (0.11)
Parental education					
< High school	980	−0.68 (0.35)	−0.15 (0.15)	−0.37 (0.34)	+0.00 (0.14)
High school	3,948	−0.06 (0.17)	−0.02 (0.07)	−0.21 (0.17)	+0.11 (0.07)
> High school	2,665	+0.31 (0.21)	+0.18 (0.08)	+0.19 (0.20)	+0.30 (0.08)
Missing	241				
Physician-diagnosed respiratory illness at <2 years old					
No	6,600	+0.05 (0.13)	−0.02 (0.05)	−0.00 (0.13)	+0.19 (0.05)
Yes	214	−1.83 (0.75)	−0.01 (0.30)	+0.35 (0.72)	−0.13 (0.29)
Missing	1,020				
History of bronchitis					
No	6,640	+0.16 (0.13)	+0.02 (0.05)	−0.15 (0.13)	+0.17 (0.05)
Yes	1,143	−1.03 (0.32)	+0.03 (0.13)	+0.11 (0.31)	+0.07 (0.12)
Missing	51				

...dicated that pulmonary function measurements at the initial examination were often lower than the predicted values, presumably due to a learning effect which occurs subsequent to this initial examination. Theoretically, this effect of first examination should be most noticeable among children with only two measurements, whose levels will be negatively biased and growth rates will be positively biased. In fact, children with only two measurements (table 2) had a statistically significant negative mean level of FEV_1 (−0.53 per cent) and a statistically significant positive mean growth rate (+0.34 per cent per year). For children with three or more visits, the mean FEV_1 level (+0.17 per cent) and mean relative growth rate (+0.02 per cent per year) were not significantly different from 0. Similar results were found for FVC (table 2).

Parental education, a measure of socio-economic status, was associated with both level and growth rate. Children whose parents were least educated had the lowest mean level and the lowest mean growth rate for both FEV_1 and FVC (table 2). Both level and growth rate increased monotonically with level of parental education. All regression analyses to test for effects of parental smoking or gas stoves were therefore adjusted for parental education.

Two indicators of early respiratory illness, reported physician-diagnosed respiratory illness before two years of age and reported history of bronchitis, were associated with significantly lower mean FEV_1 levels ($p < 0.02$ and $p < 0.001$, respectively), but not with growth rates (table 2). No associations, were found between either measure of early respiratory illness and FVC level or growth rate. These two indicators of early respiratory illness were not considered in the subsequent analyses.

Parental smoking

The mean values of FEV_1 level and growth rate by parental smoking status suggest an independent effect of each parent's smoking on both outcome variables (table 3). Children whose parents did not smoke had both the highest level and highest growth rate. A regression analysis including maternal and paternal smoking status, city of residence, and parental education gave an estimated effect of maternal smoking on FEV_1 level of -0.61 per cent ($p = 0.03$) and for paternal smoking of -0.41 per cent ($p = 0.14$) (table 4). For FEV_1 growth rate, the estimated effect of maternal smoking was -0.09 per cent per year ($p = 0.43$) and the estimated effect of paternal smoking was -0.02 per cent per year ($p = 0.87$). Since paternal and maternal smoking behavior were positively correlated, the analysis was repeated with only maternal smoking included in the model, yielding an estimated effect of -0.80 per cent ($p = 0.002$) for FEV_1 level, and -0.10 per cent per year ($p = 0.32$) for FEV_1 growth rate. A weighted regression analysis including the number of parents who smoked as the independent variable gave estimated effects of -0.47 per cent ($p = 0.003$) per smoker for FEV_1 level and -0.09 per cent per year ($p = 0.19$) per smoker for growth rate.

To assess the evidence for an exposure-response relationship, parental smoking level was then defined as the number of cigarettes smoked by each parent. A regres-

TABLE 3

Weighted means (standard errors) of pulmonary function levels and growth rates (deviations from predicted), of 7,834 children by parental smoking habits and stove type

Variable	No.	FEV₁ Level (%)	FEV₁ Growth rate (%/year)	FVC Level (%)	FVC Growth rate (%/year)
Parental smoking					
Neither	2,042	+0.65 (0.24)	+0.15 (0.10)	−0.02 (0.23)	+0.21 (0.09)
Father only	1,877	+0.26 (0.25)	−0.04 (0.10)	−0.36 (0.24)	+0.16 (0.10)
Mother only	738	+0.02 (0.40)	−0.08 (0.15)	−0.06 (0.39)	−0.06 (0.15)
Both	2,484	−0.54 (0.22)	+0.01 (0.09)	+0.08 (0.21)	+0.15 (0.08)
Missing	693				
Maternal smoking (cigarettes/day)					
0	4,208	+0.45 (0.17)	+0.06 (0.07)	−0.18 (0.16)	+0.21 (0.06)
1–5	431	+0.41 (0.52)	+0.36 (0.20)	−0.30 (0.50)	+0.49 (0.19)
6–15	916	−0.14 (0.36)	−0.13 (0.14)	−0.20 (0.35)	+0.05 (0.14)
16–25	1,446	−0.79 (0.29)	+0.02 (0.11)	+0.19 (0.28)	−0.00 (0.11)
26–35	534	−1.86 (0.47)	−0.23 (0.19)	−0.82 (0.46)	+0.03 (0.18)
36–45	202	−0.55 (0.77)	−0.32 (0.31)	+0.72 (0.74)	+0.08 (0.30)
46+	53	+1.31 (1.52)	+0.44 (0.65)	+0.87 (1.46)	+0.48 (0.61)
Missing	44				
Stove type					
Electric	3,698	+0.29 (0.18)	−0.02 (0.07)	+0.48 (0.17)	+0.10 (0.07)
Gas	3,360	−0.27 (0.19)	+0.06 (0.07)	−0.65 (0.18)	+0.19 (0.07)
Both	563	−0.12 (0.45)	+0.08 (0.17)	−0.48 (0.44)	+0.26 (0.17)
Missing	213				

TABLE 4

Regression coefficients (in per cent, with standard errors) for four different measures of parental cigarette smoking and for gas stove exposure in explanatory models for level and growth rate of ln(FEV₁) and ln(FVC)

Variable	FEV₁		FVC	
	Level	Growth rate	Level	Growth rate
*Measures of exposure to parental smoking**				
Model 1				
Maternal smoking status	−0.61 (0.27)	−0.09 (0.11)	0.46 (0.27)	−0.14 (0.11)
Paternal smoking status	−0.41 (0.28)	−0.02 (0.11)	−0.12 (0.27)	0.09 (0.11)
Model 2				
Maternal smoking status	−0.80 (0.25)	−0.10 (0.10)	0.34 (0.25)	−0.13 (0.10)
Model 3				
No. of smokers	−0.47 (0.16)	−0.09 (0.07)	0.16 (0.16)	−0.02 (0.07)
Model 4				
Maternal smoking level (packs/day)	−0.81 (0.21)	−0.17 (0.09)	0.33 (0.21)	−0.17 (0.08)
Exposure to gas stove†				
Presence of a gas stove	−0.41 (0.32)	0.09 (0.13)	−0.56 (0.31)	0.06 (0.12)

* All models include city and parental education.
† All models include city, parental education, and maternal smoking status.

sion analysis including maternal smoking level, city of residence, and socioeconomic status gave an estimated effect on FEV_1 level of −0.81 per cent ($p = 0.0001$) and on growth rate of −0.17 per cent per year ($p = 0.05$) per pack of cigarettes (table 4). These results are qualitatively consistent with those achieved using parental smoking status but more highly significant, as would be expected when substituting a measured for a discrete exposure variable. The maternal smoking level is a measure of total cigarettes smoked per day by the child's mother, and may overestimate smoking in the home. The reversal seen at 46+ cigarettes per day (table 3) may be due to the small sample size in this group and overestimation of the child's exposure. When considered alone, paternal smoking level was not a significant predictor of level or growth rate.

No statistically significant associations were found between FVC values and parental smoking status (table 4). The estimated effect of maternal smoking level on FVC level was +0.33 per cent per pack ($p = 0.12$) and the estimated effect on growth rate was −0.17 per cent per year per pack ($p = 0.04$).

Gas cooking

Mean values of the pulmonary function measures were calculated for children exposed to only one stove type and for children exposed to both electric and gas stoves (table 3). Weighted regression analysis controlling for amount of maternal smoking as well as for city and parental education found no significant associations between gas stove exposure and pulmonary function measures (table 4). The estimated effects of gas stove exposure on pulmonary function level were −0.41 per cent ($p = 0.41$) for FEV_1 and −0.56 per cent ($p = 0.07$) for FVC. Stove type was not significantly associated with pulmonary function growth rates.

DISCUSSION

Although numerous cross-sectional studies have found an association between childhood respiratory health and parental smoking habits, those studies have been unable to assess the degree to which pulmonary function growth rates may be affected by exposure to sidestream cigarette smoke. Tager et al. (16) in a longitudinal study reported that children exposed to one

pack per day of maternal smoking experienced significant deficits in FEV_1 growth rate which resulted in an estimated cumulative deficit in FEV_1 level of 173 ml by adult life relative to children of nonsmoking mothers. This represents a deficit of 3 to 4 per cent in maximum attained level of FEV_1 in early adult life.

Our data indicate that children of mothers smoking one pack per day have an estimated 0.81 per cent lower FEV_1 level at eight years of age than children of nonsmoking mothers ($p = 0.0001$). Furthermore, the estimated effect on FEV_1 growth rate is -0.17 per cent per pack per year of exposure between ages six and 10 ($p = 0.05$). This corresponds to a deficit in FEV_1 growth rate of about 3 ml between the eighth and ninth birthdays for a boy with an initial FEV_1 of 1.62 liters. It also implies a 1.14 per cent lower FEV_1 by age 10, or about 21 ml for a child whose predicted FEV_1 level in the absence of smoking exposure is 1.90 liters. Extrapolation of this effect to age 20 would imply a cumulative effect of 2.8 per cent. Although these results are consistent in direction with the findings of Tager et al. (16) in their study based in East Boston, MA, the estimated effect of maternal smoking on FEV_1 growth rate is only marginally significant in our data, and the size of that effect during the preadolescent years is substantially smaller than reported by Tager et al. This difference may be explained in part by a more substantial effect of parental smoking during adolescence, which cannot be observed in our preadolescent data. The use by Tager and colleagues of a nonlinear model which implies that the largest effect occurs in the early years of exposure is also a factor in the contrasting results for preadolescents. Our model assumes that the incremental effect of exposure to a certain level of cigarette smoking, expressed in percentage terms, is independent of age and exposure history. The relatively brief follow-up interval of four years analyzed for this report does not allow discrimination between

these linear and nonlinear exposure-response models. Although the estimated associations between paternal smoking and FEV_1 measurements were similar in direction to those seen for maternal smoking, they were consistently smaller and failed to achieve statistical significance.

The observed association of both FEV_1 level and rate of growth with current maternal smoking behavior could be explained either as a consequence of prenatal and early childhood exposure, which shifted children toward a lower track of pulmonary function growth, or as an effect of exposure during the period of follow-up. Presumably, most women who smoked during the period of follow-up had also smoked when their children were quite young, although some may have abstained during pregnancy. Indeed, only 400 of 7,834 mothers reported a change in smoking status between the first and last examination, an interval of two to four years.

To distinguish between the effects of current and early childhood exposure to cigarette smoke would require follow-up, preferably beginning during pregnancy or in early childhood, of a group of children whose exposure varied substantially over the period of follow-up. In the extreme, if mothers remained either smokers at a fixed smoking level or nonsmokers during the entire period from conception to adulthood of their children, current and early childhood exposure would be identical and no such separation of effects would be possible. This is nearly the case in this study, in that few mothers reported a qualitative change in smoking status during the study, and changes in reported smoking level were presumed to be due in large part to variability in reporting. Although several analyses were attempted to assess the effects of changes in smoking level from year to year after controlling for average exposure during the period of follow-up, these analyses showed that the available information was insufficient for this purpose.

The observed associations between FVC

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values and parental smoking behavior were somewhat different. A statistically significant positive association between maternal smoking and FVC had been seen in earlier cross-sectional analyses of data from the first two examinations (7), but the longitudinal data indicate that this positive association was smaller and no longer statistically significant by eight years of age due to a significant negative association between maternal smoking level and FVC growth rate. These results suggest that, if parental smoking leads to increased FVC levels in children up to age six, these effects may disappear as children mature. This pattern contrasts with the apparent increase in the cumulative effect of passive smoking on FEV_1 as children mature.

Other cross-sectional studies have reported increased FVC levels in children exposed to cigarette smoke (25). In a recent report of physiologic measurement in infants, children of smoking mothers had larger functional residual capacities than comparable infants of nonsmoking mothers (26). Lung size has also been found to be increased in offspring of rats who received nicotine throughout pregnancy (27). The relevance of these findings to the observed association between FVC level and passive smoking is uncertain, however, and the association may be a chance occurrence.

Our data suggest that exposure to gas stoves has comparable effects on FEV_1 and FVC. Previous analyses had detected significantly lower levels of both pulmonary function indices at the first examination among children living in homes with gas stoves (7). The longitudinal data, however, show a small and nonsignificant positive association between gas stove use and pulmonary function growth rates, so that by the age of eight years the association between gas stove exposure and FVC level, while still negative, was not statistically significant. These data could be interpreted as suggesting an effect of gas stove exposure among the youngest children which is partially reversible. For the present, however, this interpretation can be only tentative. The limitations of classification by stove type as a surrogate for measured exposure to nitrogen dioxide or other emission products are now widely recognized. Studies using personal monitoring have shown that less than 5 per cent of the interindividual variation in levels of measured NO_2 is explained by stove type, while up to 60 per cent can be explained by measurements in the home (28). Thus, future studies of NO_2 exposure should incorporate indoor or personal monitoring.

The results reported here are based upon a large sample of preadolescent children followed for a relatively short period of time. Nevertheless, they suggest that the effects on FEV_1 of exposure to parental cigarette smoking may be cumulative during the preadolescent years. Moreover, children whose pulmonary function level is reduced due to early environmental exposures may show normal growth in percentage terms but a growing deficit in absolute terms (liters) relative to the levels that would have been achieved in the absence of early effects. Thus, these data are consistent with the hypothesis that children with deficient lung function levels in early childhood fail to reach their full pulmonary function potential. One prevalent hypothesis is that adults who are at risk of developing obstructive airways disease upon exposure to risk factors such as personal cigarette smoking come in large part from the pool of persons affected by childhood exposures. Indeed, data obtained retrospectively in adult samples suggest that childhood events are associated with adult disease (29, 30).

Insight into the validity of this hypothesis will come from continued follow-up and evaluation of these children, particularly as they pass through adolescence. Personal cigarette smoking will, unfortunately, become a factor for 20 per cent of these children (31). The data collected from these children will provide an opportunity to assess the association between early child-

hood exposures and the response to personal cigarette smoking.

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Teculescu, D.B., Pham, Q.T., Varona-Lopez, W., Deschamps, J.P., Marchand, M., Henquel, J.C., Maniciaux, M. "The Single-Breath Nitrogen Test Does Not Detect Functional Impairment In Children With Passive Exposure To Tobacco Smoke" <u>Bull Eur Physiopathol Respir</u> 22: 605-607, 1986.

ABSTRACT: Respiratory symptoms and pulmonary function were compared in 46 nonsmoking children aged 10 to 16 years, whose parents were smokers, and an identical number of children (matched for sex, age and height) whose parents were nonsmokers. Passive exposure to parental tobacco smoke resulted in a higher prevalence of respiratory symptoms, more frequent upper airway infections and a significant decrease in forced expiratory flows; these effects were more marked in boys. The single-breath nitrogen washout test, a sensitive test of small airways obstruction in adults, did not detect any effect of involuntary smoking in this limited sample of children.

THE SINGLE-BREATH NITROGEN TEST DOES NOT DETECT FUNCTIONAL IMPAIRMENT IN CHILDREN WITH PASSIVE EXPOSURE TO TOBACCO SMOKE

LE RINÇAGE DE L'AZOTE EN RESPIRATION UNIQUE NE DÉTECTE PAS D'ANOMALIE FONCTIONNELLE CHEZ LES ENFANTS EXPOSÉS PASSIVEMENT À LA FUMÉE DE TABAC.

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ABSTRACT: Respiratory symptoms and pulmonary function were compared in 46 nonsmoking children aged 10 to 16 years, whose parents were smokers, and an identical number of children (matched for sex, age and height) whose parents were nonsmokers. Passive exposure to parental tobacco smoke resulted in a higher prevalence of respiratory symptoms, more frequent upper airway infections and a significant decrease in forced expiratory flows; these effects were more marked in boys. The single-breath nitrogen washout test, a sensitive test of small airways obstruction in adults, did not detect any effect of involuntary smoking in this limited sample of children.

Forced expiration; passive smoking in children; single-breath nitrogen test.

Children with involuntary (passive) exposure to tobacco smoke in their homes were reported to have more respiratory infections in the first year of life [6], more respiratory symptoms [5], more frequent tonsillopharyngitis [13] and frequent hospital admissions for severe respiratory disease during childhood [10]. Some impairment of their pulmonary function, by analogy to that described for adults with passive exposure at work [21], could be expected, but the results of such studies were controversial [20]. In most studies, only the conventional measurements of forced vital capacity (FVC) and forced expiratory volume in one second (FEV_1) were obtained, although wide agreement exists as to their poor sensitivity in detecting early airflow limitation [11]. Among others, the single-breath washout nitrogen (SBN_2) test was proposed as a more sensitive means for detecting small airway dysfunction [2]. We here present a preliminary report of lung function measurements (SBN_2 test and maximal expiratory flows) in children with or without passive exposure to tobacco smoke in their homes.

SUBJECTS AND METHODS

Children and adolescents aged 10 to 16 years, attending a Preventive Medicine Centre with their families for a medical check-up, were asked to participate in a study of determinants of pulmonary function if they had no known chronic disease and came from an area without significant air pollution; between June and November 1983, 535 children volunteered. The ATS-DLD questionnaire [9], supplemented with questions on tobacco consumption by the child and a history of acute respiratory infections in the last two months was completed (interview of one parent by the physician). The FVC, FEV_1, forced expiratory flows at 50 (FEF_{50}) and 25% (FEF_{25}) (to be expired) of vital capacity were measured with a pneumotachograph (Fleisch no. 3) and integrator connected to a microcomputer (Apple II). At least three satisfactory trials were required, the best result being recorded; the predicted values were those of ZAPLETAL *et al.* [22]. The slope of the alveolar N_2 concentration (phase III - PIII) and the closing volume in per cent of the expired vital capacity (CV% VC) were measured [12] from a plot of N_2 concentration (Hewlett-Packard type 47302 A analyser) against expired volume (Fleisch no. 1 pneumotachograph + integrator) by a microcomputer (Apple II) using an algorithm derived from that of CRAVEN *et al.* [7]. The SBN_2 was always done after the forced expiration to allow the validation of the slow vital capacity; two satisfactory trials were required and the mean value was retained. Statistics used the x^2 test with Yates's correction for small samples and the Student t-test.

RESULTS

Among the 505 children with complete questionnaires and at least the forced expiration test, we identified 52 who had both parents smokers. Six of these

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Table II. — Anthropometric data and predicted values of pulmonary function tests

	Two parents smoke	
	Yes	No
Sex distribution (boys/girls):	23/23	23/23
Age (yr)	12.74 ± 1.47	12.82 ± 1.58
Height (cm)	153.3 ± 9.7	152.7 ± 8.8
Weight (kg)	41.52 ± 8.65	41.43 ± 8.20
Predicted FVC (ml)	2945 ± 628	2900 ± 517
Predicted FEV$_1$ (ml)	2627 ± 495	2588 ± 402
Predicted FEV$_1$/FVC (%)	89.6 ± 3.3	89.6 ± 3.4
Predicted FEF$_{50}$ (ml·s^{-1})	3628 ± 527	3585 ± 495
Predicted FEF$_{25}$ (ml·s^{-1})	1983 ± 269	1967 ± 239

$\bar{x}$ ±SD. All the differences are non-significant. For abbreviations in tables I and II, see text.

children were active smokers themselves and were excluded, leaving 46 (23 girls) for analysis. Each 'case' was matched for sex, age and height with a nonsmoking child whose parents were nonsmokers ('control'). The matching was satisfactory as no significant differences existed for anthropometric variables and for predicted values of ventilatory function (table I). The observed values of FVC and forced flows were larger in children whose parents were nonsmokers (table II), but the differences were either small (e.g. 36 ml for FVC) or, when larger, represented a small part of intersubject variability (e.g. 301 ml·s^{-1} for FEF$_{50}$ equalled only 0.33 of the standard deviation of the group of 'control' children). The mean values of phase III N$_2$ slope and closing volume were similar for the two groups. Children whose parents smoked were slightly taller; this explains why FEV$_1$ and FEF$_{50}$ expressed as percent of predicted are significantly (5% level, Student t-test) lower in this group.

Chronic cough or sputum production were present in 9 'cases' and 3 'controls'; although the gradient is large, numbers are too small for significance (corrected x^2 (Yates)=2.39). An acute respiratory infection in the two months preceding the study was present in 20 'cases' and 7 'controls', this association being significant at the 1% level (corrected x^2=7.54)

Table II. — Observed values of pulmonary function tests

	Two parents smoke		Significance (t-test)
	Yes	No	
FVC (ml)	3007 ± 697	3043 ± 547	NS
(% pred)	102.2 ± 10.0	105.4 ± 11.9	NS
FEV$_1$ (ml)	2689 ± 564	2769 ± 504	NS
(% pred)	102.3 ± 9.7	107.1 ± 12.1	p < 0.05
FEV$_1$/VC (%)	89.9 ± 5.4	91.1 ± 4.3	NS
(% pred)	100.3 ± 5.6	101.7 ± 5.2	NS
FEF$_{50}$ (ml·s^{-1})	3502 ± 792	3803 ± 911	NS
(% pred)	96.7 ± 17.9	106.8 ± 25.1	p < 0.05
FEF$_{25}$ (ml·s^{-1})	1841 ± 566	2007 ± 559	NS
(% pred)	92.9 ± 26.2	101.7 ± 23.8	NS
Slope of Phase III (%N$_2$·l^{-1})	1.126 ± 0.418*	1.041 ± 0.386**	NS
CV/VC (%)	3.77 ± 3.17*	3.89 ± 2.60**	NS

$\bar{x}$ ± SD. * only 34 children with valid results; ** only 42 children with valid results.

DISCUSSION

Our main objective was to evaluate the yield of the SBN$_2$ test in detecting early abnormality in children with passive exposure to tobacco smoke. Before the analysis of the entire sample of children in respect to the smoking habits of their parents, we did the preliminary study reported here, in which only the extreme conditions (both parents smokers or both parents nonsmokers) were considered in a matched-pair approach. The result was clearly negative: the slightly higher (0.08% N$_2$·l^{-1}) PIII in children 'at risk' was due to an isolated high value (2.98% N$_2$·l^{-1}) in a girl; in boys, PIII was practically identical for the two groups (1.031 and 1.044% N$_2$·l^{-1} respectively). Incidentally, we wish to stress the fact that inability to perform the SBN$_2$ test was much more frequent among girls 'at risk' (10 of 23) than in the 'control' group (3 of 23); this difference was not found for boys. Thus, our preliminary results in children using a computerized SBN$_2$ determination do not confirm the results obtained with manual calculations in adult smokers in whom PIII and CV%VC were significantly increased in subjects with normal spirography [4, 14].

The negative result was not due to the absence of any influence of paternal smoking on the respiratory condition of their children. The answers to the questionnaire indicate a threefold difference in the prevalence of chronic dry and/or productive cough in exposed children; the difference was due to the subgroup of boys in whom 8 'cases' against 2 'controls' had chronic cough or sputum. There was a significant (p < 0.01) association between a history of recent upper airway infection and exposure to tobacco smoke at home; the gradient between the two groups was found in girls (9 vs 3) and boys (11 vs 4) as well. These findings are in agreement with those of BLAND et al. [3] and DODGE et al. [8] for the prevalence of respiratory symptoms and of CAMERON et al. [5] for the increase in susceptibility to respiratory infections.

The ventilatory function of passive smoking children was slightly impaired. Low numbers did not allow validation of minimal differences for indices like FVC; when differences were larger, intersubject variability was a limiting factor for significance. It is rather surprising, in these circumstances, to find significant differences such as those found by us for FEV$_1$ and FEF$_{50}$. When the forced expiration variables were compared by sex, no difference was significant for girls (although FEF$_{50}$ was 12% lower in exposed girls 103... 85% pred 15.6±29.9% pred p=0.10) when in boys (98.4±8.4% pred vs 105.6±9.6% pred t=2.58 p<0.02 and FEF$_{25}$ (80.8±19.1 vs 97.1±21.1% pred t=2.74 p<0.01) were significantly reduced in exposed boys. Thus, the matched-pair approach allowed us to confirm, in a relatively small group of children, the ventilatory function impairment due to passive exposure to tobacco smoke previously reported in large epidemiologic studies [18, 19]. As in the study of TASHKIN et al. [15], the effect of parental smoking was present

mainly in boys; the reasons for the increased suscept-
ibility of airways of males are not clear. In one recent
study [19], the decrease in forced flows of children
showed the expected dose-response relationship with
parental tobacco consumption, but, quite unexpect-
edly, the forced vital capacity was (significantly) posi-
tively related to the amount of tobacco smoked by
their parents [16].

Parental smoking effects on children's lung func-
tion are very complex. The recent Official Statement
of the American Thoracic Society Board of Directors
[1] discusses: 1) the effects of maternal smoking *dur-
ing pregnancy* (probably due to absorption of toxins
such as carbon monoxide and nicotine) resulting in
an increased rate of abnormal placental implant-
ation, premature delivery, reduced birth weight,
increase in neonatal deaths from asphyxia; 2) the
effects of *passively inhaled smoke* on respiratory
symptoms and lung function in childhood (for extens-
ive review, see [20]).

The decrease of forced flows and a higher preval-
ence of respiratory symptoms are possibly due to
passive exposure to cigarette smoke in their homes
in the children investigated by us. However, many
other factors (educational, social, genetic, etc.) may
exert an influence. A higher proportion of children
of smokers had a history of recent acute respiratory
infection, and this was found to influence pulmonary
function of adults even after disappearance of respi-
ratory symptoms [17]. Thus, we cannot exclude an
indirect influence of parental smoking on the pul-
monary function of children, through the impairment
of the respiratory tract defence mechanisms. The
possible influence of the factors mentioned above will
be taken into account in the final analysis of the
results of our study.

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RÉSUMÉ: La prévalence des symptômes respiratoires et l'atte-
inte fonctionnelle respiratoire ont été comparées chez 46 enfants
non fumeurs âgés de 10 à 16 ans, dont les parents étaient fumeurs,
et chez un nombre identique d'enfants (appariés pour le sexe,
l'âge et la taille) dont les parents étaient non-fumeurs. L'exposi-
tion passive au tabagisme parental est accompagnée d'une fréqu-
ence plus élevée des symptômes respiratoires, d'infections respira-
toires aiguës et d'une réduction significative des débits expiratoires
forcés; ces effets sont plus prononcés chez les garçons. Le test
de rinçage de l'azote en respiration unique, un test sensible de
l'obstruction des voies aériennes périphériques chez l'adulte, n'a
pas permis de détecter d'anomalie dans cette étude préliminaire
portant sur un nombre limité d'enfants.

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Chen, Y., and Li, W.X. "The Effect of Passive Smoking on Children's Pulmonary Function in Shanghai" Am J Public Health 76: 515-518, 1986.

The authors studied the relationship between passive smoking and pulmonary function of 571 children in Shanghai, People's Republic of China. The children studied ranged in age from 8 to 16 years. Questionnaires were completed by the children's parents, and lung function tests were administered to the children. Paternal smoking status during the child's lifetime was linearly related to a decrease in the percent predicted values of FEV1.0, MMEF, and FEF62.5-87.9 in all subjects; in school girls, paternal smoking accounted for 0.5 percent, 1.2 percent, and 1.6 percent of the total variation for these lung function parameters respectively. The trend was reportedly less marked in boys. Other environmental factors considered in this study included educational level of the father, the use of coal or gas for cooking, and the presence of patients with chronic respiratory diseases in the family. These other factors reportedly had "no important role on the children's pulmonary function."

The Effect of Passive Smoking on Children's Pulmonary Function In Shanghai

YUE CHEN, BM, AND WAN-XIAN LI, MD

Abstract: We report the findings of a cross-sectional study of the relationship between passive smoking and pulmonary function of children in Shanghai, People's Republic of China. The 571 study subjects included 303 males and 268 females, ranging in age from 8 to 16 years, from a primary school and a secondary school at Xu-Hui District. Lung function tests were performed at the schools, and questionnaires were completed by parents. The father's cigarette smoking status during child's lifetime was linearly related to a decrease in the per cent predicted values of $FEV_{1.0}$, MMEF and $FEF_{62.5-87.5\%}$ in total subjects; in school-girls, father's smoking status accounted for 0.5 per cent, 1.2 per cent, and 1.6 per cent of the total variation, respectively; the trend was less marked in boys. Other environmental factors considered in this study, i.e., educational level of the father, the use of coal or gas for cooking, the presence of patients with chronic respiratory diseases in the family, etc., did not seem to have any important role on the children's pulmonary function. (*Am J Public Health* 1986; 76:515-518.)

Introduction

It has been suggested that the smoking habits of individuals in a household adversely affect the health of non-smoking family members through exposure to tobacco combustion products in the indoor environment.[1,2] Sidestream smoke, which rises from the burning end of the cigarette and produces approximately 70 per cent of the air pollution due to tobacco smoke in a room, contains even greater concentration of some toxic compounds than mainstream smoke exhaled by smokers.[3-5] Children of smoking parents have been observed to have reduced pulmonary function.[6-10] A dose-response relationship has been found in some studies,[6-8] but other studies failed to find an association between children's pulmonary function and the smoking habits of their parents.[11-14] Methodological and data processing differences may be responsible for these conflicting results.

We report the findings of a cross-sectional investigation in Shanghai using stepwise regression and other methods in data analysis.

Methods

Subjects

A total of 571 children (303 males and 268 females) 8 to 16 years of age from a primary school and a middle school at Xu-Hui District in Shanghai participated in this cross-sectional study in June 1984. The residential area of sample selection is so small that it is reasonable to consider the level of outdoor urban air pollution to be the same for all residents.*

Pulmonary Function Test

Lung function tests of the children were performed at schools using two 8-liter water-filled recording spirometers. The children did not wear nose clips, and the tests were performed in a sitting position. Good understanding and cooperation were usually obtained. Each child was tested until three acceptable curves were obtained. The two best forced vital capacity's (FVCs) of the three acceptable curves should not vary by more than ±10 per cent in reading or ±100 ml, whichever is greater. The single best curve, which has maximal forced expiratory volume in one second ($FEV_{1.0}$), was used in the analysis. FVC, $FEV_{1.0}$, maximal midexpiratory flow (MMEF), and forced expiratory flow from 62.5 per cent to 75.5 per cent of FVC ($FEF_{62.5-87.5\%}$) were read from this best tracing. Values were corrected to body temperature and pressure saturated with water vapor (BTPS). Each child was free from any cough, cold, or sore throat at the time of testings. Standing height, weight, and chest measurement (CM) by the end of expiration were measured at the same time.

Questionnaire Administration

The children's parents completed a questionnaire providing information on their smoking habits and those of other household members over the child's lifetime, on demographic characteristics, medical history, the use of coal or gas for cooking, average household residential area per capita, and father's education.

Smoking habits of the children were obtained from another questionnaire, completed in the classroom and returned to the investigator at once. Children who reported smoking one or more cigarettes per week were rare and were excluded from analysis, as were children with a history of asthma or congenital heart disease.

Data Analysis

Stepwise regression analysis was applied to a model including 12 terms, spelled out in the Appendix. Spirometric indexes (FVC, $FEV_{1.0}$, MMEF, and $FEF_{62.5-87.5\%}$) were analyzed separately for male and female. F value to enter and remove was fixed to the level of $\alpha = 0.05$. Appropriate transformations and a parametric test of normality[15] for the original data of spirometric indexes were done (data available on request to author).

Results

Table 1 displays the results of the stepwise analysis. The transformed FVC is closely related to age, standing height and chest measurement in males, and with standing height and chest measurement in female, accounting for 79 per cent and 68 per cent of the total variation, respectively; there are no associations with any environmental factors in either sex at the level of the fixed F value chosen in advance. Because flow depends on volume,[16] and because the relationship between father's smoking status and the FVC of children did not reach the 0.05 level, the data were also controlled for

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*The annual average mediums of SO_2, NO_3, Pb, and P in the Xu-Hui District are 0.07, 0.02, 0.000428, and 0.24 mg/m³, respectively. The maxima in 1984 were 0.59, 0.09, 0.00907 and 0.40 mg/m³.

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TABLE 1—Analysis for Transformed FVC

Stepwise Regression Analysis	Factors Selected				
	Male			Female	
	Age	Ht.	CM	Ht.	CM
b*	0.0078	0.0039	0.0035	0.0051	0.0055
S_b*	0.0025	0.0005	0.0007	0.0006	0.0009
R†	0.8871			0.8269	

*Partial regression coefficient.
*Standard error of partial regression.
†Multiple correlation coefficient.

FVC when the three other spirometric indexes were analyzed in order to compensate for differences in lung size.

Table 2 shows the results of the transformed $FEV_{1.0}$, MMEF, and $FEF_{62.5-87.5\%}$ regressions for males. In addition to the physical characteristics and FVC, father's smoking quantity (cigarettes/day × years) during the children's lifetime accounted for 0.1 per cent, 0.5 per cent, and 0.8 per cent of the total variation separately. The remaining environmental factors did not show significant effects on boys' lung function. The trend was more marked in females. For a girl aged 12 years, of average height, weight, and chest measurement (147 cm, 37 kg, 66 cm), the predicted $FEV_{1.0}$, MMEF, and $FEF_{62.5-87.5\%}$ were 1.78 liter, 2.24 liter/sec, and 1.32 liter/sec if the father smoked 10 cigarettes a day for 10 years during the girl's lifetime, and 1.84 liter, 2.38 liter/sec and 1.45 liter/sec if he did not smoke. In addition, the use of gas for cooking in family showed a negative relationship with transformed $FEF_{62.5-87.5}$ per cent of females.

In order to compare and clarify the results, the per cent of predicted values of $FEV_{1.0}$, MMEF, and $FEF_{62.5-87.5}$ per cent of the two sexes were calculated. The prediction equations for lung function of each sex were derived from the data of the total survey population. From these equations, the proportion of the total variation, which is explained by age, height, weight, chest measurement and FVC, is determined. The regressions for the per cent of predicted values of $FEV_{1.0}$, MMEF, and $FEF_{62.5-87.5\%}$ plotted as functions of father's smoking quantity in child's lifetime are shown in Figure 1. The slope of the lines are not the same. The lines of $FEF_{62.5-87.5\%}$ decrease more rapidly than the others.

The average residential area per capita was 5.3 m^2 for nonsmoking father families and 5.1 m^2 for smoking father families; the average number of persons per family was 4.2.

Discussion

Two earlier findings reported by Tager and his associates[5] and by Weize and his coworkers[7] have shown results similar to ours: the greater the number of smokers at home, the lower the MMEF value of the child, although these studies lacked quantitative estimates of lifetime passive smoke exposure. In another study, Hasselblat[8] found a significant correlation between the amount smoked by the mother and $FEV_{0.75}$ value of her child, but the amount smoked by father was not related to the child's pulmonary function test. The authors felt that smoking information of the mother might be more accurate than that of the father and that the mother might spend more time with her child.[8] In Shanghai, cigarette smoking is very rare among young women in general, and no mothers in our study reported that they smoked. Other household smokers could be sources of passive smoking but there were very few identified in our study. The smoking rate of other persons in families was 6.0 per cent, while the father's smoking rate was 39.2 per cent.

The hazardous effect of cigarette smoking on the health of passive smokers depends not only on the number of cigarettes smoked in the families but also on ventilation and the volume of enclosed space.[7] Because living space in the urban area of Shanghai is so small, the actual amount of indoor exposure to children may be substantially greater than in many other areas of the world. Although exposure may have been more intense, its effect could not be measured because virtually all children lived in crowded quarters. It has been reported that the ventilation rates in warm areas of the US are higher and the smoke may be more easily diluted by the air than in generally colder areas.[13] This was another modifying factor that we were unable to measure.

Determination of the rate at which air flows out of the lungs during FVC provides important information about the resistance to airflow during forced expiration.[17] Our results showed an obstructive pattern[16] and suggested that exposure to cigarette smoking may have more obstructive than restrictive effect on the lungs as Tager, et al,[7] and Weiss et al,[6] have reported.

Our data show that the effect of passive smoking is greater in schoolgirls than in boys. Schoolboys may spend more time outdoors than schoolgirls, and thus be less exposed to indoor smoking.

There were no important effects on the lung function of children of the other environmental factors considered in our

TABLE 2—Analysis for Transformed $FEV_{1.0}$, MMEF, and $FEF_{62.5-87.5}$ in Male Children

Stepwise Regression Analysis	Factors Selected												
	$FEV_{1.0}$				MMEF			$FEF_{62.5-87.5}$					
	Ht.	ESF	SQF	FVC	Ht.	SQF	FVC	Age	Ht.	Wt.	CM	SQF	SQO	FVC
b	.0012	.0066	-.0012	.1152	.0024	-.0059	.0996	.0125	.0096	-.0090	.0069	-.0096	.0133	.0844
S_b	.0004	.0043	.0015	.0071	.0009	.0035	.0170	.0062	.0020	.0034	.0037	.0050	.0084	.0259
R	.9215				.7117			.8891						

ESF = Educational Status of Father.
SQF = Smoking Quantity of Father.
FVC = Forced Vital Capacity.
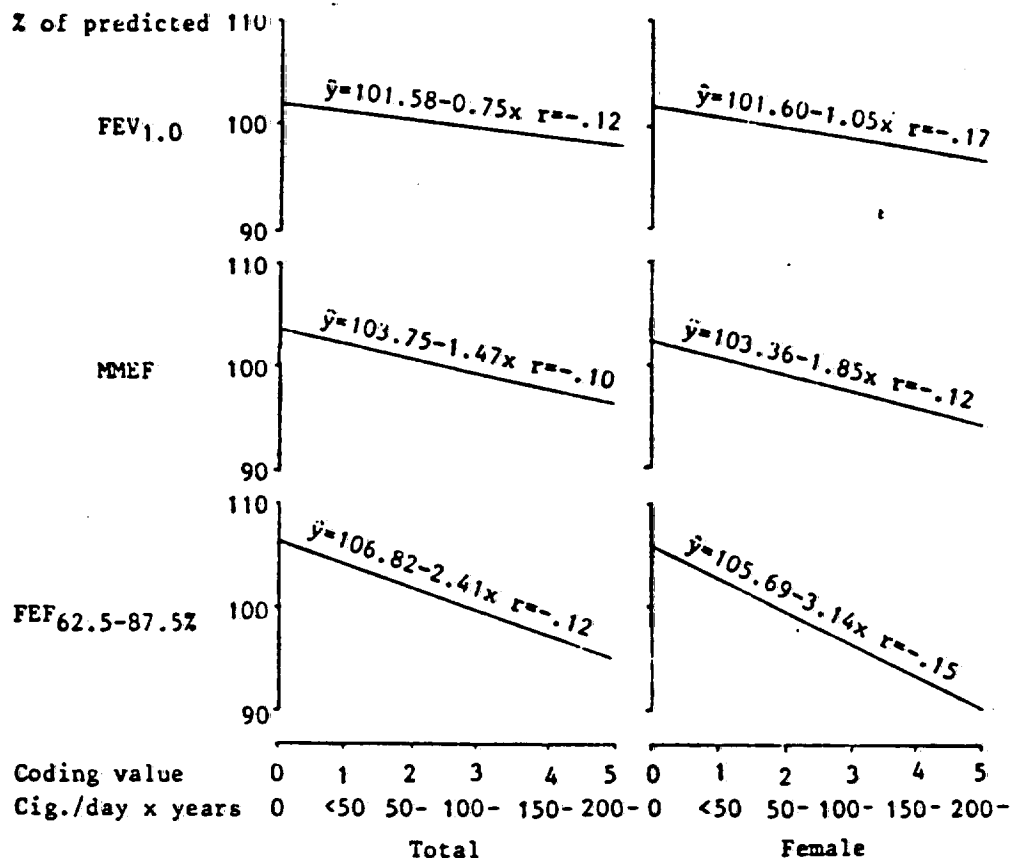CM = Chest Measurement.
SQO = Smoking Quantity of Others.

% of predicted

$FEV_{1.0}$: Total: $\tilde{y}=101.58-0.75x \quad r=-.12$; Female: $\tilde{y}=101.60-1.05x \quad r=-.17$

MMEF: Total: $\tilde{y}=103.75-1.47x \quad r=-.10$; Female: $\tilde{y}=103.36-1.85x \quad r=-.12$

$FEF_{62.5-87.5\%}$: Total: $\tilde{y}=106.82-2.41x \quad r=-.12$; Female: $\tilde{y}=105.69-3.14x \quad r=-.15$

Coding value: 0 1 2 3 4 5 / 0 1 2 3 4 5

Cig./day x years: 0 <50 50- 100- 150- 200- / 0 <50 50- 100- 150- 200-

Total   Female

FIGURE 1—Adverse Effect of Father Smoking on Lung Function of Children.

study. The slight difference of per cent predicted values of $FEV_{1.0}$, MMEF, and $FEF_{62.5-87.5\%}$ among different groups of girls classified according to father's educational level may denote that the smoking rate was lower for men with university level education (27.9 per cent) than those with secondary or primary schooling (44.7 per cent and 57.1 per cent, respectively). When we adjusted for father's education, the effects of passive smoking were still evident.

Several studies have reported that using coal for cooking is more harmful to children's health than using gas.[19] In this survey, only a small number of households (14.5 per cent) used the coal-fueled stove at home, and the influence of coal could not be detected.

It has also been suggested that the presence of respiratory symptoms in children is not only associated with parental smoking, but also with respiratory symptoms among parents.[14,20] In our study, the presence of patients with chronic respiratory diseases in the family did not affect the lung function of children.

It has been reported that tobacco smoke can be a significant source of atmospheric pollution in enclosed areas.[25] This cross-sectional survey offers new evidence that

TABLE 3—Analysis for Transformed $FEV_{1.0}$, MMEF, and $FEF_{62.5-87.5\%}$ in Female Children

Stepwise Regression Analysis	Factors Selected											
	$FEV_{1.0}$				MMEF				$FEF_{62.5-87.5\%}$			
	HL	WL	BOF	FVC	HL	WL	BOF	FVC	HL	BOF	Gas	FVC
b	.0012	-.0007	-.0021	.0714	.0066	-.0055	-.0157	.2077	.0073	-.0193	-.0668	.1168
Sb	.0002	.0003	.0008	.0039	.0024	.0026	.0078	.0393	.0018	.0075	.0357	.0357
R	.9125				.8628				.8966			

See Table 2 for acronyms.

passive smoking may constitute a real threat to the health of many urban children. Passive smoking is not only associated with lower levels of pulmonary function but also with the occurrence of both acute respiratory illness and chronic respiratory symptoms in children.[1] Concern for the health of their children could be a strong incentive to encourage smoking parents to quit and nonsmokers not to start.

APPENDIX

Variables Used in Regression Analysis

1. Age (years)
2. Standing height (centimeters)
3. Weight (kilograms)
4. Chest measurement (centimeters)
5. Educational status of father (university: 263, secondary: 287, primary: 21)
6. Smoking quantity of the father during the child's lifetime (never: 346, less than 50 cigarettes/day × years: 69, 50- cigarettes/day × years: 50, 100- cigarettes/day × years: 57, 150- cigarettes/day × years: 16, 200- cigarettes/day × years: 33)
7. Smoking status of other individuals in the family (no: 538, yes: 33)
8. Use coal for cooking (no: 488, yes: 83)
9. Use gas for cooking (no: 84, yes: 487)
10. Average residential area per capita (square meters)
11. Presence of patient with chronic respiratory diseases in family (no: 501, yes: 70)
12. FVC (liter, considered when $FEV_{1.0}$, MMEF, and $FEF_{25-75\%}$ were analyzed)

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ABSTRACT. The relationship of passive smoking to respiratory
conditions and pulmonary function was assessed using a cross-
sectional design in the defined population of Tecumseh, Michigan.
The study population was made up of 3,482 children who were 0 to
19 yr of age at the 1962-1965 examination and for whom questionnaire
information was available for both parents. Nearly 62% of children
in this age group were exposed at the time of examination to at
least 1 parent who smoked. Passive exposure to cigarette smoke
was associated with an elevated prevalence of phlegm, wheeze,
asthma, and chest colds among males and wheeze, bronchitis, and
chest colds among females. Using logistic regression, offspring
were shown to be 1.5 to 2.0 times more likely to have a respiratory
condition if both their parents currently smoked than if both
parents never smoked. FEV1 and FVC among males and Vmax50 among
females were significantly lower by 5% in nonsmokers 10 to 19 yr
of age whose parents were current smokers compared with similar
offspring of never smoking parents. Respiratory conditions were
generally more frequent and the level of lung function was generally
lower for males from households where only mothers smoked compared
with males from households where only fathers smoked, although
sample size was limited. In females similar relationships were
less consistent. Differences tended to be larger and more often
significant for males than for females when respiratory symptoms
and illness were examined. Comparisons between offspring of 2
current and 2 never smoking parents and those involving the number
of parental smokers in a child's lifetime provided stronger
associations of passive smoking with respiratory conditions and
lung function than did the number of household smokers, duration,
or amount of parental smoking. In general, these associations
were independent of parental education, family size, parental
reporting bias, and the child's own smoking habits.

Passive Smoking in Childhood

Respiratory Conditions and Pulmonary Function in Tecumseh, Michigan[1-4]

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Introduction

Until recently, relatively few studies have focused on the health effects of passive or involuntary smoking. Passive smoking during infancy and childhood has been associated with acute respiratory illness (1-16), chronic respiratory symptoms (17-22), and reduced pulmonary function (21, 23-26), although not all investigations have confirmed these associations (27-31). The qualitative and quantitative differences of mainstream and sidestream cigarette smoke have been documented (32, 33); a number of constituents are more concentrated in sidestream than in mainstream smoke. The need for better characterization of exposure and control of potential confounding factors has been recognized (34-37).

Investigations involving young children are of interest for several reasons: (1) confounding effects of active smoking and occupational exposures are absent, (2) children may be more exposed and/or susceptible than adults, and (3) the risks of passive exposure can be assessed during the period of lung growth and development. Children spend 60 to 80% of their time indoors (38), depending on season and geographic location. Because cigarette smoking is prevalent among adults, the likelihood of passive exposure in children is high. It has been estimated that 54 to 70% of children are exposed to one or more cigarette smokers in the household environment (1, 27, 28, 38, 39). Because of the large number of exposed persons, the proportion of time spent indoors and recent energy conservation efforts, the public health impact of passive smoking could be substantial.

The purpose of this study was to assess the cross-sectional relationships of passive smoking to respiratory symptoms, illnesses, and lung function in children and adolescents of Tecumseh, Michigan. Several measures of passive smoking were developed from questionnaire data. Effects of parental education, family size, parental symptoms and illnesses, and active smoking by the children themselves are evaluated.

Methods

Study Population

Residents of Tecumseh, Michigan have been participants in a community-based prospective investigation for the past 25 yr. The major purpose of the Tecumseh Community Health Study has been to identify determinants of health and disease in a natural community. Its design, methods, and historical perspective have been described previously (40-42). Standard questionnaires, certain physiologic measurements, and clinical assessments by physicians were available.

During the second cycle of examinations, conducted between 1962 and 1965, a total of 4,378 children and adolescents 0 to 19 yr of age were interviewed and examined. Of the 4,378 subjects, the following were excluded from this investigation: 82 because they were not residing with their parents, 688 because both parents were not interviewed, and 126 because they were active smokers (smoking habits were available only for those 16 to 19 yr of age; children 15 yr of age or younger were assumed to be nonsmokers). A total of 3,482 nonsmoking males and females 0 to 19

SUMMARY The relationship of passive smoking to respiratory conditions and pulmonary function was assessed using a cross-sectional design in the defined population of Tecumseh, Michigan. The study population was made up of 3,482 children who were 0 to 19 yr of age at the 1962-1965 examination and for whom questionnaire information was available for both parents. Nearly 82% of children in this age group were exposed at the time of examination to at least 1 parent who smoked. Passive exposure to cigarette smoke was associated with an elevated prevalence of phlegm, wheeze, asthma, and chest colds among males and wheeze, bronchitis, and chest colds among females. Using logistic regression, offspring were shown to be 1.5 to 2.0 times more likely to have a respiratory condition if both their parents currently smoked than if both parents never smoked. FEV_1 and FVC among males and $Vmax_{50}$ among females were significantly lower by 5% in nonsmokers 10 to 19 yr of age whose parents were current smokers compared with similar offspring of never smoking parents. Respiratory conditions were generally more frequent and the level of lung function was generally lower for males from households where only mothers smoked compared with males from households where only fathers smoked, although sample size was limited. In females similar relationships were less consistent. Differences tended to be larger and more often significant for males than for females when respiratory symptoms and illnesses were examined. Comparisons between offspring of 2 current and 2 never smoking parents and those involving the number of parental smokers in a child's lifetime provided stronger associations of passive smoking with respiratory conditions and lung function than did the number of household smokers, duration, or amount of parental smoking. In general, these associations were independent of parental education, family size, parental reporting bias, and the child's own smoking habits.

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yr of age and members of their households constituted the study population.

Questionnaire

Personal, demographic, and medical information were ascertained using a standard questionnaire. Parents responded for children 15 yr of age or younger. Several respiratory symptoms and illnesses were selected for evaluation: these included cough, phlegm, wheeze, asthma, bronchitis, and colds settling in the chest. In general, questions involved a past history of these conditions, rather than ascertainment of symptoms and illnesses defined only at the time of interview. Specific questions used to define these respiratory conditions and results concerning neonatal, allergic, and other conditions are reported elsewhere (43). The diagnostic criteria for asthma, reported by Higgins and Keller (44) and Broder and coworkers (45), were used, and a probable or suspect diagnosis was included as asthma.

Information was available concerning parental education, family size, and presence or absence of parental respiratory symptoms or illness. Categories of parental education included: (1) at least one parent who did not complete high school, (2) both parents completed high school, and (3) either parent attended college. Family size was defined as the number of persons residing in a household. Categorical definitions were used to classify children according to whether their mothers or fathers had a history or diagnosis of the specific respiratory condition under study.

Pulmonary Function

A Wedge® spirometer (Med-Science Electronics, Burlington, MA) and a two-channel recorder (Sanborn Co., Waltham, MA) operating at a paper speed of 25 mm/s were used to measure lung function. Following maximal inspiration, subjects performed several maximal expiratory efforts until 2 satisfactory tracings were obtained. Measurements of volume and flow were based on the tracing with the largest vital capacity and were adjusted to body temperature and pressure saturated with water vapor (BTPS).

Seven volume and flow measurements were available (46); forced expiratory volume in one second (FEV_1), forced vital capacity (FVC), and forced expiratory flow at 50% of vital capacity ($Vmax_{50}$) were selected for use in this study because they have been used in other studies and were available at subsequent examinations. Lung function analyses reported here involved young persons 10 to 19 yr of age in 1962 through 1965.

Measures of Passive Smoking

Children were classified by smoking habits of their household members at the time of interview. Only cigarette smoking and not pipe or cigar smoking was taken into account. Five measures of passive smoking were developed.

I. Current and Past Parental Smoking Habits:

Father:	Never	Current	Current	Never	All
Mother:	Never	Current	Never	Current	Others

II. Number of Parental Smokers During Child's Lifetime: (0, 1, and 2).

III. Number of Current Household Smokers: (0, 1, 2, 3, or more).

IV. Duration of Parental Smoking During Child's Lifetime.

V. Current Amount of Parental Smoking.

The first index provided one of the more extreme contrasts in passive smoke exposure, where children having both parents who never smoked are compared with those having both parents who were current smokers. Children from households where only fathers smoked and where only mothers smoked could also be compared using this index. The "all others" category included children having one or both parents who were former smokers. For the second index, children were categorized by presence or absence of parental smoking during the child's lifetime. To include potential prenatal exposure to parental smoking, a child's lifetime was defined as 1 yr before birth to the time of examination in 1962-1965. Smoking habits of siblings and relatives who were 16 yr of age or older were included with those of parents in the classification of current household smokers. For duration and amount of parental smoking, the number of years and average number of cigarettes smoked per day by each parent were summed.

Data Analysis

Prevalence rates of respiratory symptoms and illnesses, and levels of lung function in children and adolescents were compared across parental smoking categories using 5-yr, age- and sex-specific groups. Stratification was used initially to control for potential confounding by parental education, family size, parental history of respiratory symptoms or illness, and active smoking by adolescents. Significance was assessed using standard t and chi-square tests for differences between means and proportions, respectively. Age-adjusted prevalence rates were derived using the age distribution of all nonsmoking subjects 0 to 19 yr of age examined in 1962-1965 as a standard. A Cochran/Mantel-Haenszel procedure was used to test for the average partial association between passive smoking and a specific respiratory symptom or illness, controlling for the effects of age group and assessing whether a linear trend exists (47). To compare age-adjusted means, variances for those having or not having a specific respiratory condition were calculated, and a standard z statistic for comparing means with known but unequal variances was used to determine significance.

Multiple logistic regression (48) was employed to control for potential confounders simultaneously. Sex-specific analyses were performed using each respiratory condition as the response variable. The number of parental smokers during a child's lifetime (0, 1, 2) was selected as the independent variable of primary interest and was coded using 2 indicator variables. Parental education, family size, parental symptom or illness, as well as age of the child were considered as covariates. For asthma a diagnosis of hay fever and history of other allergies were also included in the model as potential predictors. Several methods of including age were considered; regression coefficients were similar for each. Likelihood ratio tests (48) were used to compare methods of including age, to decide whether certain variables should be retained in the logistic model, and to confirm whether or not statistical interaction was present. Goodness of fit for these logistic models was assessed using methods proposed by Lemeshow and Hosmer (49), where information from both cases and noncases is incorporated.

Levels of lung function were expressed as a percent of predicted or were adjusted using analysis of covariance. Predicted values of FEV_1, FVC, and $Vmax_{50}$ were obtained by regressing observed values of asymptomatic nonsmokers on age and height separately for 2 age and sex groups using the population of nonsmokers 10 to 19 yr of age who were

TABLE 1

REGRESSION STATISTICS FOR LUNG FUNCTION MEASUREMENTS, ASYMPTOMATIC NONSMOKING MALES AND FEMALES, TECUMSEH, 1962-1965*

Sex	Age (yr)	Measure	Regression Statistics					
			n	a	b_1	$-b_2$	R^2	$S_{y \cdot x}$
Male	10-15	FEV_1	528	-5.293	0.115	0.043	0.747	0.423
		FVC	528	-6.447	0.118	0.052	0.739	0.507
		$Vmax_{50}$	516	-4.311	0.152	0.038	0.490	0.729
	16-19	FEV_1	127	-3.722	—	0.046	0.289	0.534
		FVC	127	-6.214	—	0.064	0.303	0.720
		$Vmax_{50}$	124	-1.226	—	0.034	0.075	0.890
Female	10-15	FEV_1	524	-3.888	0.093	0.032	0.550	0.396
		FVC	524	-4.322	0.096	0.038	0.559	0.437
		$Vmax_{50}$	514	-2.816	0.112	0.031	0.264	0.754
	16-19	FEV_1	155	-3.397	—	0.040	0.233	0.432
		FVC	155	-3.305	—	0.041	0.220	0.459
		$Vmax_{50}$	154	-2.134	—	0.037	0.054	0.940

* Regression model: Predicted lung function = $a + b_1 \cdot$ age (yr) + b_2 (height in cm) for 10- to 15-yr-olds; predicted lung function = $a + b_2 \cdot$ height (cm) for 16- to 19-yr-olds.

TABLE 2

PREVALENCE OF PARENTAL SMOKING AMONG
SUBJECTS 0 TO 19 YR OF AGE, TECUMSEH,
1962-1965

Parental Smoking			
Father	Mother	n	%
Never	Never	567	15.7
Current	Current	1,136	31.5
Current	Never	983	27.2
Never	Current	109	3.0
All others		813	22.5
Total		3,608	99.9

free of asthma and wheeze without colds, and if 16 to 19 yr of age, free of cough, phlegm, and moderate or severe shortness of breath. A total of 1,357 nonsmokers 10 to 19 yr of age met these criteria and had complete age, height, and lung function data (FEV$_1$, FVC, or Vmax$_{50}$). The significant terms of the selected regression model included age and height for those 10 to 15 yr of age and height only for those 16 to 19 yr of age. Regression statistics for these models are presented in table 1. Models that included powers of height, weight, or interaction terms did not increase substantially the amount of variation explained by the simple model employing only age and height. Race was not included in the models because all subjects are white. Regression statistics for FEV$_1$ and Vmax$_{50}$ were published previously for nearly the same group of children 10 to 15 yr of age (50). Sex-specific regressions were used because of differences between males and females in lung growth.

Analysis of covariance models were also used to adjust levels of lung function for age and height, parental education, and family size (51). The covariance model assumes no interaction and a linear relationship between covariates and lung function. Tests for equality of slopes among those exposed and unexposed to parental smoking were performed to rule out interaction; linearity was also assessed. Both assumptions for the model were met (43). In contrast to the percent of predicted method of adjustment, this approach does not require definition of a healthy

standard population and allows comparisons to be made in units of actual lung volume or flow.

Results

Prevalence of Passive Smoking

Prevalence of passive exposure to cigarette smoke was estimated using two-parent households where both parents were interviewed (table 2). A total of 61.7% of all subjects 0 to 19 yr of age had at least one currently smoking parent; 31.5% had both parents who currently smoked. Having a father as the only parental smoker was far more prevalent than having a mother as the only parental smoker (27.2% versus 3.0%). Only 15.7% of the subjects 0 to 19 yr of age were never exposed to parental smoking.

Respiratory Symptom and Illness Prevalence

Prevalence rates of several respiratory symptoms and illnesses in Tecumseh have been shown previously to vary with age and sex (43). Age-specific prevalence rates of several respiratory conditions are presented in table 3. For most respiratory conditions, prevalence rates tended to be higher in males than in females, significantly so for phlegm, wheeze, asthma, and chest colds in at least one of the age groups. Cross-sectional frequencies of phlegm, wheeze, and chest colds tend to decrease as age increases, whereas with cough, asthma and bronchitis prevalence rates vary with age in a less consistent manner. Age-adjusted prevalence rates of 4 respiratory conditions are presented by parental smoking category for males and females in figures 1 and 2, respectively. For both sexes and all 4 conditions, prevalence rates were higher among nonsmoking children whose parents both currently smoked than among children whose parents never smoked. Differences
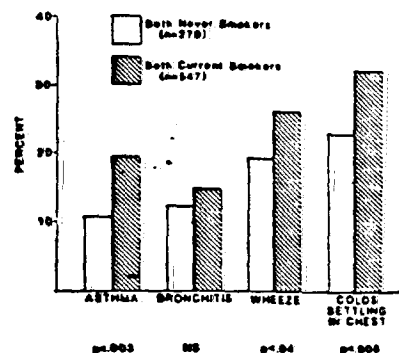

Fig. 1. Age-adjusted prevalence of respiratory conditions by parental smoking, male nonsmokers 0 to 19 yr of age, Tecumseh, 1962-1965.

were significant for the majority of conditions.

When the number of parental smokers during a child's lifetime was considered, age-adjusted prevalence rates were highest for children exposed to 2 parental smokers and generally lowest for unexposed children, the trend being significant for phlegm, wheeze, asthma, and colds settling in the chest among males and for wheeze, bronchitis, and colds settling in the chest among females (table 4). Although not presented in detail here, for all respiratory conditions except bronchitis in males, parents of nonsmokers 0 to 19 yr of age reported smoking significantly more cigarettes (mean differences ranged from 1 to 4 per day) and for significantly longer periods of time (mean differences ranged from 7 to 24 months) when a given respiratory symptom or illness was reported for their children than when it was not reported, after adjusting for differences in age (p < 0.0001).

Previous work in Tecumseh has shown that parental smoking habits are related to parental education but not to family size (43, 52). In this investigation, level of education was highest among households where both parents never smoked. Although not shown here, children from households where both parents currently smoked tended to have higher respiratory symptom and illness prevalence rates than those where both parents never smoked within each degree of parental education and family size.

When results were stratified by parental history of a given respiratory condition, there was some reduction in the magnitude of the parental smoking effect, yet for several conditions the relationship remained significant. For example, in households where both parents

TABLE 3

PREVALENCE (%) OF RESPIRATORY SYMPTOMS AND ILLNESSES BY AGE AND SEX, NONSMOKING
CHILDREN FROM TWO-PARENT HOUSEHOLDS, TECUMSEH, 1962-1965*

Respiratory Condition	0-4		5-9		10-14		15-19	
	M (n = 470)	F (n = 491)	M (n = 555)	F (n = 540)	M (n = 482)	F (n = 460)	M (n = 241)	F (n = 243)
Cough	7.6	8.6	10.7	9.5	10.8	7.6	7.3	7.8
Phlegm	18.4	13.5†	14.1	14.9	13.7	9.7	8.5	8.9
Wheeze	31.7	24.9†	20.6	18.5	18.5	15.0	17.9	16.2
Asthma	13.6	10.7	16.2	9.2‡	17.0	9.7‡	13.3	8.2
Bronchitis	13.3	10.5	15.9	12.6	11.0	10.0	11.7	14.5
Chest cold	39.9	30.4‡	29.4	26.5	20.9	19.0	19.2	14.9

* Differences tested between males and females within each age group using chi-square.
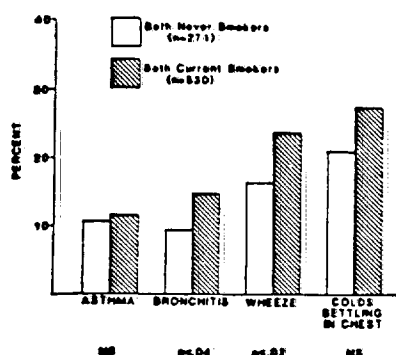† p < 0.05.
‡ p < 0.01.
§ p < 0.001.

Fig. 2. Age-adjusted prevalence of respiratory conditions by parental smoking, female nonsmokers 0 to 19 yr of age, Tecumseh, 1962-1965.

reported a history of phlegm, male offspring had a prevalence rate for phlegm of 13.4, 12.5, and 18.5% for 0, 1, and 2 parental smokers, whereas the prevalence rate was 14.9, 9.0, and 17.5%, respectively, when both parents denied history of phlegm. Differences remained significant for phlegm and asthma among males regardless of a history of the same symptom or illness in their parents.

Results obtained using logistic regression models are presented in table 5. The odds ratios represent measures of the degree of association between passive smoking and each respiratory condition controlling for potential confounding by age, parental education, and family size. For example, the odds of a male 0 to 19 yr of age having asthma are 2.16 times as great if he was passively exposed to 2 parents who currently smoked than if he was unexposed. For both sexes and almost all respiratory conditions, odds ratios were higher for children with 2 parental smokers compared with children who had never been exposed to parental cigarette smoke. Odds ratios tended to be higher for males from households where mothers were the only smokers than for males from households where only fathers smoked. The pattern was reversed, though less consistently, for females.

When logistic regression models employing the number of parental smokers during a child's lifetime (0, 1, or 2) were used as a measure of passive smoking, similar odds ratios were obtained for most respiratory conditions. When children with one parental smoker were compared with the unexposed reference group, odds ratios were frequently close to or less than 1.0, yet did not differ significantly from 1.0. This suggests that exposure to one parental smoker, who was

most often the father, is not associated with an increased probability of having these respiratory symptoms or illnesses. In comparing logistic models using the 2 different passive smoking measures, the −2 log likelihood values and the fraction of variance explained by the models are almost identical, suggesting that little is gained statistically by categorizing parental smoking more completely with 5 as opposed to 3 levels (43). An analysis of the goodness of fit for these logistic models revealed close agreement between observed and expected cases across deciles of risk.

Pulmonary Function

Mean lung function expressed as a percent of predicted is presented in figure 3 for nonsmoking males and females 10 to 19 yr of age whose parents were both

never (98 males and 93 females) or current (201 males and 199 females) smokers. Mean FEV_1 and FVC for males and $\dot{V}max_{50}$ for females were significantly lower if both parents were current smokers rather than never smokers. Results were virtually identical when 10- to 14- and 15- to 19-yr-old age groups were analyzed separately.

Levels of FEV_1 and FVC for males and $\dot{V}max_{50}$ for females were inversely related to the number of parental smokers during a child's lifetime among nonsmokers 10 to 19 yr of age. Using analysis of covariance to adjust levels of lung function for age and height, male nonsmokers 10 to 19 yr of age from households where both parents smoked had a mean FEV_1 that was 144 ml (4.6%) lower than that for males with no parental smokers (table 6). Similarly, a deficit of 173 ml (4.9%) in

TABLE 4

AGE-ADJUSTED PREVALENCE (%) OF RESPIRATORY CONDITIONS BY SEX AND NUMBER OF PARENTAL SMOKERS DURING CHILD'S LIFETIME, NONSMOKERS 0 TO 19 YR OF AGE, TECUMSEH, 1962-1965*

	Males			Females		
	Number of Parental Smokers			Number of Parental Smokers		
Respiratory Condition	0 (n = 339)	1 (n = 718)	2 (n = 681)	0 (n = 360)	1 (n = 716)	2 (n = 646)
Cough	8.6	8.4	11.4	8.4	8.0	8.7
Phlegm	13.4	12.8	18.8†	8.7	13.5	13.6
Wheeze	20.9	20.4	26.5†	16.0	17.3	22.9‡
Asthma	13.4	11.3	20.9§	9.8	7.9	11.7
Bronchitis	12.0	11.9	15.2	8.8	11.3	13.2†
Chest cold	23.4	27.6	32.0‡	20.0	22.4	27.4‡

* Generalized Cochran/Mantel-Haenszel test for average association in three-way contingency tables.
† p < 0.05.
‡ p < 0.01.
§ p < 0.001.

TABLE 5

ODDS RATIOS RELATING PARENTAL SMOKING TO RESPIRATORY CONDITIONS ADJUSTING FOR THIRD VARIABLES USING MULTIPLE LOGISTIC REGRESSION; NONSMOKING MALES AND FEMALES 0 TO 19 YR OF AGE, TECUMSEH, 1962-1965*†

		Parental Smoking				
Sex	Respiratory Condition	Father: Never Mother: Never	Current Current	Current Never	Never Current	All Others
Male	Cough	1.0	1.38	0.89	0.66	1.20
	Phlegm	1.0	1.62‡	0.93	1.77	1.15
	Wheeze	1.0	1.47‡	1.04	1.42	1.21
	Asthma	1.0	2.16‡	0.84	1.37	1.19
	Bronchitis	1.0	1.23	0.88	1.46	1.03
	Chest cold	1.0	1.56‡	1.16	1.30	1.37
Female	Cough	1.0	1.17	1.06	0.95	1.30
	Phlegm	1.0	1.43	1.92‡	0.81	1.44
	Wheeze	1.0	1.60‡	1.01	1.41	1.10
	Asthma	1.0	1.05	0.65	1.16	0.79
	Bronchitis	1.0	1.75‡	1.61	0.73	0.74
	Chest cold	1.0	1.39	1.19	0.90	1.00

* Odds ratios are relative to the reference category where both parents were never smokers.
† Third variables include age, parental education, and family size for all except asthma where age, hay fever, and other allergies were used.
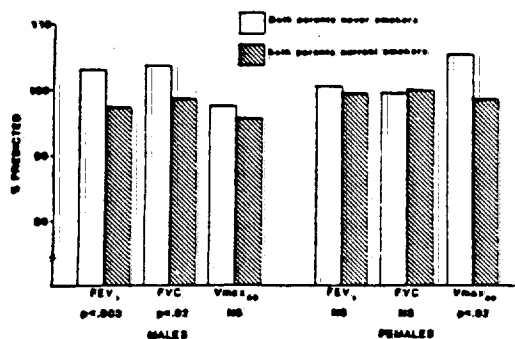‡ Significant at p < 0.05.

Fig. 3. Mean % predicted lung function by parental smoking, male and female nonsmokers 10 to 19 yr of age, Tecumseh, 1962-1965.

FVC for males 10 to 19 yr of age and of 185 ml/s (5.1%) in $Vmax_{50}$ for females 10 to 19 yr of age was observed.

Although not presented here, mean level of lung function tended to be inversely related to the total number of smokers in the household; this was most evident for FEV_1% predicted among male nonsmokers, yet sample size was small, and trends were not significant (43). Lung function was also inversely related to duration and amount of parental smoking among nonsmoking males 10 to 19 yr of age but not among females (43).

Differences in lung function across parental smoking categories were similar in magnitude when results were stratified across levels of parental education and family size. When each potential confounder was included in an analysis of covariance, model associations between passive smoking and impaired lung function persisted.

Discussion

Prevalence rates of respiratory conditions and level of lung function have been examined in a defined community for nearly 3,500 young persons in relation to the smoking habits of their parents. The prevalence of passive exposure to cigarette smoke in Tecumseh during the 1962-1965 time period was similar to that found in other population surveys (1, 27, 39). Approximately 62% of those 0 to 19 yr of age in this study had at least one parent who currently smoked compared with 54 to 70% reported in other studies. Given the large proportion of children exposed, the amount of time spent indoors, especially by younger age groups, and recent energy conservation efforts, which reduce ventilation, the public health impact of passive smoking could be substantial.

Several indirect measures of passive exposure to household cigarette smoke were developed from questionnaire data. Most investigations to date have used either a dichotomous classification or the number of current parental smokers as exposure variables; only one study defined exposure to parental smoking with reference to the child's lifetime (25). A few studies have classified exposure based on the number of cigarettes currently smoked per day (5, 9, 18, 53). Although results of this investigation were generally similar for all measures of passive smoking, current and past smoking habits and the number of parental smokers during a child's lifetime were most useful in assessing passive smoking and respiratory outcomes. Misclassification of exposure was a potential problem both for this investigation and others preceding it. The frequency of contact between children and their parents while cigarette smoking occurred, as well as exposure patterns in day care settings for young children of working parents, are additional factors that should be addressed in future research.

Passive exposure to cigarette smoke was associated with increased prevalence of phlegm, wheeze, asthma, and colds settling in the chest among males, and wheeze, bronchitis, and colds settling in the chest among females in Tecumseh. Several cross-sectional studies have demonstrated significant associations between parental smoking and phlegm (17), wheeze (17, 21), bronchitis (5-7), and asthma (12, 15), whereas others have not documented such associations (16, 27). The lack of significant association between parental smoking and history of cough in this study was consistent with results of several studies (16, 27) but not with those of others (17-19, 22). Cameron and Robertson (4) were among the first to suggest that differences in illness prevalence related to parental smoking might be of greater magnitude in geographic locations where more time is spent indoors because of the climate.

The significant inverse relationship observed in this investigation between parental smoking and level of lung function in nonsmokers 10 to 19 yr of age is consistent with several previous studies (21, 23-26, 54) but not with others (17, 27, 28, 30). Most of the studies showing a positive association also demonstrated a dose-response relationship. Results of

TABLE 6

MEAN (± SE) LUNG FUNCTION IN CHILDREN ADJUSTED FOR AGE AND/OR HEIGHT USING ANALYSIS OF COVARIANCE BY NUMBER OF PARENTAL SMOKERS, TECUMSEH, 1962-1965*

Sex	Age (yr)	Parental Smokers (n)	Examined (n)	FEV_1 (L)	FVC (L)	$Vmax_{50}$ (L/s)
Male	10-14	0	70	2.812 ± 0.047	2.824 ± 0.055	3.105 ± 0.083
		1	197	2.582 ± 0.028	2.875 ± 0.033	3.227 ± 0.049
		2	180	2.480 ± 0.030	2.790 ± 0.034†	3.060 ± 0.057
	15-19	0	41	4.210 ± 0.084	4.841 ± 0.108	4.666 ± 0.141
		1	106	4.067 ± 0.052	4.843 ± 0.067	4.611 ± 0.088
		2	75	4.052 ± 0.062	4.828 ± 0.080	4.499 ± 0.105
	10-19	0	111	3.139 ± 0.043	3.565 ± 0.053	3.626 ± 0.074
		1	303	3.060 ± 0.026	3.466 ± 0.032	3.686 ± 0.045
		2	255	2.995 ± 0.028‡	3.392 ± 0.035‡	3.537 ± 0.049
Female	10-14	0	85	2.373 ± 0.048	2.579 ± 0.053	3.365 ± 0.094
		1	181	2.380 ± 0.028	2.593 ± 0.032	3.238 ± 0.056
		2	169	2.368 ± 0.029	2.581 ± 0.033	3.187 ± 0.058
	15-19	0	50	3.041 ± 0.057	3.267 ± 0.062	4.074 ± 0.127
		1	109	3.003 ± 0.039	3.246 ± 0.042	3.852 ± 0.086
		2	72	3.039 ± 0.048	3.285 ± 0.051	3.853 ± 0.106
	10-19	0	115	2.807 ± 0.037	2.818 ± 0.040	3.614 ± 0.076
		1	290	2.802 ± 0.023	2.826 ± 0.025	3.457 ± 0.048
		2	241	2.809 ± 0.025	2.835 ± 0.028	3.429 ± 0.052†

* Defined during child's lifetime excluding smokers 16 to 19 yr of age
† $p < 0.05$
‡ $p < 0.01$

this research tend to support these findings for several measures of lung function, although the minimal level at which an effect of parental smoking can be detected remains unclear. Investigators have suggested that the lack of association observed in several studies may be due to climatic factors (17, 27), selection of a pulmonary function measure (peak expiratory flow), which may not be adequately sensitive (30), or small sample size (55). Schilling and coworkers (28) did not show a significant relationship in general, although significantly lower maximal flow at 50% of FVC (MEF_{50} or $Vmax_{50}$) was observed among nonsmoking girls whose mothers smoked. Tager and coworkers (55) suggested that a larger sample might have revealed a similar relationship among boys.

Measures of lung function in Tecumseh children were not entirely independent, because values for children of the same household were correlated. Intraclass correlation coefficients of approximately 0.25 have been observed between siblings, with 0.46 between male siblings and 0.66 between female siblings in Tecumseh (44). When a random sample of one child per household was selected from this population, results were essentially unchanged, demonstrating that a lack of independence would not account for the observed association with passive smoking.

Several investigators have adjusted children's lung function by their parent's lung function (28) or by their parent's body mass (56). It is likely, as suggested by Weiss and associates (57), that this adjustment would mask a true passive smoking effect, should it exist.

Several investigators have attempted to control for potential confounders of the relationship between passive smoking and respiratory outcomes. For example, Fergusson and colleagues (5) demonstrated an increase in bronchitis and/or pneumonia during the first 2 yr of life in children of mothers who smoked after controlling for socioeconomic status, family size, and maternal age. Several investigators have shown that the association of passive smoking with impaired lung function remains significant after controlling for parental education (23, 24), sibship size (21, 23), and the child's own smoking (25). Results from this study indicate that associations of parental smoking with prevalence of respiratory conditions and lung function are independent of parental education and family size.

Cigarette smoking by children may be related to both parental smoking and the respiratory outcomes under study. In this research, significant relationships between measures of passive smoking and respiratory outcomes have been demonstrated among children and adolescents who were presumed to be never smokers. There is a possibility that some of the observed passive smoking effect in children 10 to 15 yr of age might be due to unreported active smoking, and some of the effect in those 16 to 19 yr of age might be due to inaccurate reporting of their smoking habits. In subsequent analyses, subjects who were reexamined 15 yr later and reported cigarette smoking at an age that was younger than their baseline examination in 1962-1965, were also excluded and, in general, results were unchanged. It is unlikely that observed associations between respiratory conditions and parental smoking among the youngest age groups could be explained by active smoking by the children themselves.

Parents who smoke and report respiratory symptoms or illnesses themselves may tend to overreport respiratory conditions in their children; this parental reporting bias has been raised as a possible explanation for passive smoking health effects (6, 7, 16, 17, 27, 57). Schenker and associates (16) suggested that associations between passive smoking and respiratory symptoms and illnesses may be due to shared genetic and/or environmental factors, or to overreporting by symptomatic parents for their children. Weiss and colleagues (58) found an increased risk of atopy in nonsmoking children of smoking mothers that was not explained by maternal reporting bias. When stratification or logistic regression was used in the present research to control for parental reporting bias, trends were occasionally diminished, yet relationships generally remained significant.

It is possible that some of the observed association with passive smoking might be due to gas cooking or heating. The relationship between gas cooking or heating and respiratory conditions (16, 29, 53, 59-61), and associations with lung function have been demonstrated in some studies (23, 29) but not in others (54, 55, 59, 62). Results of a pilot study involving a sample of 213 nonsmoking women from Tecumseh did not show a significant relationship between gas cooking and FEV_1 (62). Schenker and associates (16) did not find gas cooking to be an independent risk factor for chronic respiratory symptoms or illnesses.

In general, respiratory conditions were more prevalent and, although not reported here, lung function was lower for male offspring when the only smoker in a household was the mother rather than the father (43). Stronger associations with maternal smoking than with paternal smoking have been observed in a number of studies (5, 15, 16, 21, 23, 53-55, 61, 63, 64). This is consistent with a potentially greater passive exposure of children if their mothers smoke than if their fathers smoke, because of more time spent by offspring in the presence of their mothers during this time period. In this study, associations of passive smoking with respiratory conditions and lung function appeared stronger among younger than among older age groups and among males rather than among females. Higher prevalence rates of respiratory symptoms and illnesses have been observed among younger age groups (2, 5, 21) and among male children (21, 65). Younger age and male sex have been identified as independent risk factors for acute respiratory illnesses and chronic respiratory symptoms (16). Associations between maternal smoking and lung function were strongest among younger male children in one study (64) and among female children in others (21, 24, 26, 54).

The apparent sex difference observed in this research was not explained by a difference in dose or duration of exposure to parental smoking. Confounding by active smoking could account for some of the significant associations observed in males 10 to 15 yr of age if a greater proportion of males than of females were active smokers. However, such confounding would not account for such associations in the younger age groups. As suggested by Taussig and coworkers (66), the sex differential in response to parental smoke exposure may have a physiologic basis. The higher prevalence and incidence of asthma among males, for example, may be consistent with an increased susceptibility of males to sidestream cigarette smoke or other pollutants. Weiss and associates (58) recently demonstrated significantly elevated odds ratios for atopy in males but not in females with a prior history of bronchiolitis or croup.

The magnitude of association between parental smoking and children's lung function appears similar to that found in other studies. Whether a decrement of 144 ml in FEV_1 (4.6%) associated with having 2, compared with no, parental smokers will become clinically significant with increasing age remains to be inves-

tigated. Tager and associates (55) recently reported a deficit in expected growth of lung function in children participating in the Six-Cities Study. Additional longitudinal studies should be conducted to further substantiate these long-term adverse effects and to quantitate the magnitude of impact that exposure to parental cigarette smoke may have on respiratory health. More accurate estimates of passive smoking using specifically designed questionnaires and biochemical markers such as cotinine in urine or saliva are needed.

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SUMMARY: The growth of pulmonary function between ages 5.5 and 25 years was determined in 1502 observations on 362 subjects from a representative population study of non-Mexican American whites in Tuscon. There was an average of 8.8 years of follow-up, with a maximum of 12. The model developed was robust for follow-up of 3-7 observations (3+ years). Respiratory illnesses and smoking had the biggest negative impact on growth of forced expiratory volume in 1 s(FEV1), Vmax50%, Vmax50%/forced vital capacity (FVC) parental smoking and airway obstructive disease (AOD) were important also. Flow measures showed present and more persistent effects of disease and smoking than did FEV1.

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PHYSIOLOGICAL CHANGES IN PULMONARY DEVELOPMENT RELATED TO PASSIVE SMOKING AND ITS INTERACTION WITH ACTIVE SMOKING*

(Childhood; parental smoking; bronchial reactivity; pulmonary function)

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SUMMARY

The growth of pulmonary function between ages 5.5 and 25 years was determined in 1502 observations on 362 subjects from a representative population study of non-Mexican American whites in Tucson. There was an average of 8.8 years of follow-up, with a maximum of 12. The model developed was robust for follow-up of 3–7 observations (3 + years). Respiratory illnesses and smoking had the biggest negative impact on growth of forced expiratory volume in 1 s (FEV_1); V_{max} 50%; V_{max} 50%/forced vital capacity (FVC) parental smoking and airway obstructive disease (AOD) were important also. Flow measures showed present and more persistent effects of disease and smoking than did FEV_1.

INTRODUCTION

Although there have been various evaluations of 'growth' of pulmonary function cross-sectionally, fewer studies have evaluated such growth through longitudinal measures [1–4]. The paper attempts to evaluate the effects of initial function, symptoms, disease during childhood, the onset of smoking, and effect of parental symptoms and smoking [5,6]. Relationships between these findings and our physiological findings in early childhood are indicated. The importance of bronchial reactivity in childhood is discussed as well.

MATERIALS AND METHODS

Subjects tested with a pneumotachograph were those enrolled in the epidemiological study of white non-Mexican American households in Tucson, described in detail elsewhere [7]. Subjects were tested in Surveys. There were a total of 1520 observations from 1972–1983 on 362 individuals aged 6–15 years at the time of their first satisfactory testing and up through their 25th birthday at the end of follow-up. The maximum length of follow-up was 12 years, and the average was 8.8 years.

The measures of pulmonary function derived were FVC, FEV_1, flow at 50% of FVC ($\dot{V}_{max}$ 50%), flow at 75% of expired FVC ($\dot{V}_{max}$ 75%). Individuals in the present data set were within 49% – 151% of predicted, using our previous prediction equations [8].

We used a composite growth model (unweighted longitudinal observations on individuals). It was a quadratic function of height and age. The final models, based on three or more observations per subject, were derived for FEV_1, $\dot{V}_{max}$ 50% and $\dot{V}_{max}$ 50%/FVC (as a measure of lung size-compensated flows): $FEV_1 = 6.844 + 0.040$ age $- 0.281$ height $+ 0.003$ height^2 ($R = 0.916$, $P < 0.001$); $\dot{V}_{max}$ 50% $= 5.489 + 0.056$ age $- 0.221$ height $+ 0.003$ height^2 ($R = 0.717$, $P < 0.0001$); $\dot{V}_{max}$ 50%/FVC $= 4.65 + 0.070$ age $- 0.0019$ age^2 $- 0.116$ height $+ 0.0008$ height^2 ($R = 0.278$, $P < 0.0001$).

The standard error of the estimate for FEV_1 for 3 or more points ranged from 0.3 to 0.5, and decreased with the number of observations; the multiple correlation coefficient increased with the number of observations from about 0.88 to 0.95 for FEV_1. Residuals from the model did not correlate with any age or size determinants, including sitting height, or arm span. End point residuals were calculated as well for all individuals aged 0 –14 years at entry with follow-up to assess risk factors.

In all methods of analysis, the number of observations was used as a measure of individual and survey variability; it related significantly but without pattern only to survey. SEE's derived for the individuals (with ≥ 3 values) or along with their own slopes, were used in the fashion of Goldstein [9,10] representing individual variability to determine contributions of risk variables to changes over time of each growth variable.

RESULTS

Residual proportions of FEV_1, $\dot{V}_{max}$ 50%, and $\dot{V}_{max}$ 50%/FVC were significantly related to symptoms in all age groups. Those who had physician-confirmed chronic bronchitis throughout the study had significantly lower outcome FEV_1 and especially lower outcome $\dot{V}_{max}$ 50%. Sex was not a significant covariate.

Both outcome FEV_1 and $\dot{V}_{max}$ 50% residuals were significantly related to the subjects' smoking habits, both before and after adjusting for other factors. The out-

TABLE I

ALL ENDPOINT V_{max} 50% RESIDUALS BY ADJUSTED[a] RISK FACTORS, AGES 0-14 AT ENTRY

Grand mean = -0.02

symptoms:	Yes	-4.38	(86)
	No	+2.46	(151)	P = 0.041
Active smoking:	Current	-7.32	(60)
	Ex	-0.02	(22)
	Never	+2.80	(155)	P = 0.034
Passive smoking:	Mother[b]	-.02	(127)
	Father only	+1.06	(65)
	Neither	-1.58	(45)	P = 0.858
Overall significance (ANOVA):		P = 0.006	

[a] Adjusted for each other factor, age (significant) and number of observations (not significant). Interactions: active × father's smoking (P = 0.072), parents' AOD × smoking (P = 0.112).
[b] Regardless of father's smoking.

comes were related to symptoms within smoking groups. Parental AOD (diagnosed emphysema, chronic bronchitis, or asthma) had additional effects on the children's smoking and symptoms, for endpoint V_{max} 50%, but not independently; the residual for current smokers with symptoms and parental history was -14.41 (95% confidence interval of -4.57 to -24.25). Parental smoking was not significant as a main effect within the multifactor analysis of variance. However, it showed a significant interaction with subjects' smoking (children smoked if parents did) and parental AOD (Table I).

TABLE II

ALL V_{max} 50%/FVC RESIDUALS RELATED TO CHILDREN'S SMOKING AND SYMPTOMS AND PARENTAL SMOKING, ADJUSTED FOR SEX AND OTHER VARIABLES

		Adjusted means[a]	
Ages 5.5-25	Symptoms		
	Yes	-3.24	
	No	+2.75	P < 0.001
	Mother's smoking		
	Current	-3.68	
	Ex		
	Never	+2.9	P < 0.012
	Children's smoking		
	Ever	-4.11	
	Never	+0.94	P < 0.019
	Overall ANOVA	P < 0.001	

[a] Adjusted for sex (P < 0.001) and each other (age was as).
[b] Father's smoking was of borderline significance (P = 0.143) and combined smoking (mother regardless of father smoking; father smoking only; neither) was significant (P = 0.002, adjusted means +0.44, +1.64, respectively).

Size compensation (V_{max} 50%/FVC) removed any further effects of age. Symptoms, smoking and parental smoking were all related to residuals after appropriate adjustments (Table II).

The individual slopes were not correlated with initial values, but were correlated with endpoint values. After the various adjustment using multifactor ANOVA, as before, only symptoms and smoking were highly related to individual slopes, especially those of V_{max} 50%.

DISCUSSION

Size-compensated flows showed the same pattern with age and by sex as shown in infants and smaller children [5,11], with females having higher flows for given volumes than males after puberty, even though males had higher volumes. Flows (V_{max} 50%) did not differ significantly by gender. As shown by others [6], abnormal peripheral function, as measured by the V_{max} 50%, persists longer, into adulthood. FVC per se was higher in males. It showed an increase related to maternal smoking (after adjusting for age, height and sex), as was found at our lab in infants [11]. Significantly FEV_1 showed a borderline trend in the other direction. Thus, most significant, long-term effects leading into adulthood are in small rather than large airways.

Children's symptomatology was related to parental history of AOD, and it modified effects of other factors. Initially measured pulmonary function was influenced by both parental factors and the children's respiratory history and growth in function was affected by these factors, the level of their initial function, and later symptomatology. This information confirms longitudinally our hypotheses that childhood respiratory trouble, and the affects of parental/familial factors are important in growth of pulmonary function [12-14].

Further, parental smoking specifically had an influence on the children's pulmonary function. It was mediated or modified especially by the individuals' smoking, as well as by symptoms, and parental history, and had a significant effect even after adjustments. (Further, passive smoking is associated with bronchial reactivity in 9 year olds, especially in those whose mothers smoked during pregnancy [14]. Passive smoking must have its major effect early in life [1], as it is significant at almost all ages, and as 'tracking' of residuals is so good, i.e., is little change between initial and outcome residuals.)

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Mexican-Americans in Tucson. There was an average of 8.8 yr of
follow-up, with a maximum of 12. The method used was shown to be
robust for span of follow-up from 3 to 12 yr (3 to 7 observations),
and the results were verified by standard statistical methods.
The standard error of the estimate decreased linearly with follow-
up, indicating th eneed for longitudinal evaluation. Respiratory
symptoms and diagnoses had the biggest negative impact on growth
of lung function, using FVC, FEV1, Vmax50, and size-compensated
flows (Vmax50/FVC). Smoking had the next biggest negative impact.
Smoking cessation was shown to have a positive impact on growth of
pulmonary function. Using a second linear model to adjust for
individual variability and the random variability over surveys,
individual growth showed similar trends. Further negative impacts
were due to parental smoking, especially as it interacts with active
smoking and respiratory disease. Flows at end of follow-up (Vmax50,
Vmax50/FVC) were more sensitive than FEV1 to the effects of
concurrent disease and smoking, and more persistent effects of
these factors in early adulthood.

Longitudinal Study of Pulmonary Function Development in Childhood, Adolescence, and Early Adulthood

Development of Pulmonary Function[1-4]

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Introduction

The study of the growth of pulmonary function in childhood and into early adulthood has stimulated many investigations. Although there have been various evaluations of this "growth" cross-sectionally, fewer studies have evaluated such growth through longitudinal measurements of pulmonary function (1-9). Many of these studies have been with only 2 observations over time. For those studies with 3 or more points in time, the basic questions relate to how to represent the generalized growth model, how growth is statistically dependent on initial measures of function, how it is related to respiratory illnesses in childhood, and the effects of active smoking, passive smoking, and other environmental factors. Basic questions are whether there are differences in growth between the 2 sexes (10), and whether airways of different sizes grow at the same rate or are affected differently by internal and external factors (11).

This report evaluates the longitudinal growth of pulmonary function in subjects who have been enrolled in the Tucson Epidemiological Study of Airways Obstructive Diseases since 1972 (12). It is a study of the development of spirometric function and the characteristics and robustness of a model of growth. The effects of sex, age, size, and of other respiratory factors on growth are examined. The report attempts to evaluate the effects of initial function, symptoms, disease during childhood, the onset of smoking, parental symptoms and parental smoking.

Methods

Subjects studied were those enrolled in the longitudinal epidemiologic study of white non-Mexican-American households in Tucson. The study has been described in detail elsewhere (12).

SUMMARY The growth of pulmonary function between 5.5 and 25 yr of age was determined using 1,511 observations over time on 353 subjects from a representative population sample of white non-Mexican-Americans in Tucson. There was an average of 8.8 yr of follow-up, with a maximum of 12. The method used was shown to be robust for span of follow-up from 3 to 12 yr (3 to 7 observations), and the results were verified by standard statistical methods. The standard error of the estimate decreased linearly with follow-up, indicating the need for longitudinal evaluation. Respiratory symptoms and diagnoses had the biggest negative impact on growth of lung function, using FVC, FEV₁, Vmax₅₀, and size-compensated flows (Vmax₅₀/FVC). Smoking had the next biggest negative impact. Smoking cessation was shown to have a positive impact on growth of pulmonary function. Using a second linear model to adjust for individual variability and the random variability over surveys, individual growth showed similar trends. Further negative impacts were due to parental smoking, especially as it interacts with active smoking and respiratory disease. Flows at end of follow-up (Vmax₅₀, Vmax₅₀/FVC) were more sensitive than FEV₁ to the effects of concurrent disease and smoking, and more persistent effects of these factors in early adulthood.
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Spirometric Testing Over Time

Subjects 5.5 yr of age or older were tested spirometrically with a pneumotachygraph, using ATS/Snowbird criteria, as described previously (13, 14). The measures of pulmonary function derived were FVC, FEV₁, flow at 50% of FVC (Vmax₅₀), and flow at 75% of expired FVC (Vmax₇₅). Their percent of predicted FEV₁ values were in the range of 49 to 151% at entry, using our previously published prediction formulas (14). Subjects were tested in Surveys 1 to 8 (February 1972 through May 1984), with the exception of Survey 4. Thus, it was possible to have a maximum of 7 observations. We required at least 3 yr of follow-up for subjects to be included in the data file. There were a total of 1,511 observations on 353 subjects 5.5 to 15 yr of age at the time of their first satisfactory testing, and the oldest was 25 yr of age at the end of follow-up. The maximum length of follow-up was 12 yr, and the average was 8.8 yr; table 1 shows the 1,511 observations divided by the number of observations per person. The height distribution by age appeared normal for a pediatric population. The age range was divided into four 5-yr intervals to evaluate cohort effects; cohorts were divided into those in an age group who had their first spirometric test either during the first 3 yr of the study (1972 to 1975) or whose first test was performed during subsequent surveys (1977 or later). Using multiple regression techniques, each pulmonary function variable was regressed against age (years, decimalized); height (in inches); and the 2 together, separately for those within each age group and by cohort. Differences were evaluated by multifactorial analyses of variance (ANOVA) as well, in which gender was a covariate. In these analyses, gender was not significant for Vmax₅₀, and was inconsistent for FEV₁. There were no significant differences between cohorts in the specific regressions in the 4 age groups (5.5 to 10 yr, 11 to 15, 16 to 20, and 21 to 25), for any of the 4 measures (FVC, FEV₁, Vmax₅₀, Vmax₇₅), as confirmed by ANOVA. The Vmax₇₅ results were highly variable, and were not used further. Thus, we studied all subjects with longitudinal data, regardless of when they entered the longitudinal study.

TABLE 1
THE NUMBER OF OBSERVATIONS PER INDIVIDUAL SUBJECT

	2	3	4	5	6	7	Total
Observations							
n	56	210	440	425	240	140	1,511
%	3.7	13.9	29.1	28.1	15.9	9.3	100.0
Subjects							
n	28	70	110	85	40	20	353
%	7.9	19.8	31.2	24.1	11.3	5.7	100.0

The effect of multiple longitudinal observations per individual subject within the different age groups was evaluated to determine the possible dependence of multiple observations in the same subjects over time. Only 4.3% of those with 3 longitudinal observations were within the same age group. Those with 3 or more longitudinal observations had 56% of such observations in 2 different age groups, 41% in 3, and 2% in 4 different age groups. Thus, individual subjects tended to have observations spread throughout the age range. The number of observations was used as a covariate in later analyses to represent each subject's contribution to those analyses.

Method of Evaluating Functional Development

The first approach chosen for the present evaluation of development ("growth") was to use all observations of all subjects over the age range in the longitudinal data set to find the best-fitting equations (using least squares). It is similar to the descriptive approaches used previously in this study (15-18). This approach is generally one of using unweighted observations per individual to evaluate each pulmonary function variable. The best fitting composite equations were curvilinear, relating to age as well as to height. The robustness of the method was determined by comparing the values derived for subgroups with differing numbers of observations. The values for those with only 2 points differed significantly from those with 3 or more observations. Therefore, those subjects with only 2 points were excluded from further analysis. The standard error of the estimate for FEV_1 by number of observations for 3 or more points ranged from 0.3 to 0.5 L, and decreased with the number of observations; the multiple correlation coefficient increased with the number of observations from about 0.88 to 0.95 for FEV_1. Thus, predicted values fit the observed values very closely. The standard error of the estimate and the multiple correlation coefficient for the $Vmax_{50}$ did not have any trend related to the number of observations.

Results of Composite Fitting

Forms of the equations and resulting predictions derived from each of the other longitudinal subsets defined by the number of observations were similar in appearance. Age (in decimalized years) and a height-height squared function (height in inches) were important overall and in all age groups. In females, height did not explain as much of variance in parameters as it did in males. Age squared was important for the curvilinear model of $Vmax_{50}/FVC$ as well.

The FEV_1 and FVC were greater for males than for females, but were a relatively constant function of height at each age. Thus, these variables and the $Vmax_{50}/FVC$ were evaluated using separate gender models (13, 14) and/or using sex as a covariable (9). Completely separate gender analyses did not contribute much useful information, and are not discussed at length.

The final curvilinear equations that best explain the development of function between 5 and 25 yr of age, based on 3 or more observations per subject, were derived for FVC and FEV_1 (in liters), $Vmax_{50}$ (liters/second), and $Vmax_{50}/FVC$ (in liters/FVC seconds, as a measure of lung size-compensated flows). They are as follows:

$$FVC = 9.17 + 0.054\ Age - 0.373\ Height + 0.004\ Height^2\ (SEE = 0.495, R = 0.923, p < 0.001).$$

$$FEV_1 = 6.844 + 0.040\ Age - 0.281\ Height + 0.003\ Height^2\ (SEE = 0.431, R = 0.916, p < 0.001).$$

$$Vmax_{50} = 5.489 + 0.056\ Age - 0.221\ Height + 0.003\ Height^2\ (SEE = 1.037, R = 0.717, p < 0.001).$$

$$Vmax_{50}/FVC = 4.65 + 0.070\ Age - 0.0019\ Age^2 - 0.116\ Height + 0.0008\ Height^2\ (SEE = 0.296, R = 0.278, p < 0.001).$$

Residuals

Residuals from the equations did not correlate with any further age, age-height, or size determinants (including sitting height and arm span). Average age did correlate with number of observations; those having the largest number of observations were an average of 1 yr younger than those having only 3 observations. This was not a factor that influenced the results.

To analyze differences related to other factors, residuals from the equations were derived for each observation and were expressed as proportions of the predicted values. Residuals are positive if above the predicted value and negative if below it; percent predicted can be calculated by adding 100% to the residual. The residuals thus derived were normally distributed within age groups and overall, and age was not a major factor in determining these distributions.

Residuals for observations of all subjects had significant autocorrelations with at least 3 prior observations of FEV_1 and $Vmax_{50}$ when entered hierarchically in multiple regressions. The simple correlation for FEV_1 values in adjacent surveys was 0.77, decreasing to 0.53 for values 3 surveys apart. Therefore, because of autocorrelations, in most analyses we evaluated the effect of factors using only the end-point residuals for each individual subject, as representing that subject's outcome value.

In addition, end-point residuals were calculated for all subjects younger than 14 yr of age at entry with any spirometric test who were 12.4 to 26.4 yr of age at the time of their last spirometry (n = 440). This allowed us to assess effects of early respiratory illnesses and effects of early exposures to tobacco smoke on end-point function.

Statistical Comparisons

Statistical analyses were performed on the DEC 10-Cyber 175 of the University Computer Center, using the SPSS statistical package, the BMDP Package (19), and custom Fortran programs.

Methods used included those of previous studies, such as multifactor analysis of variance (ANOVA) and covariance (ANCOVA) (9), and more standard evaluations of subgroup differences (3, 5, 6, 8, 15-18). Age and sex were used as covariables, as in the analyses of Ware and coworkers (9), except when specified. Analyses evaluated the independent and interactive effects of various risk factors on lung function. As height is a function of age also, and as their effects on function are combined biologically between puberty and maximum lung growth (17), interactions of these 2 were used in these analyses. Because the method used is a variant of the repeated measures ANOVA (linear model) (19, 20), the repeated measures ANOVA model was used as well (19), in part to verify the results from the method and the multifactorial ANOVA and ANCOVA.

Individual Development Curve Model

A second major approach assessing relationships between other factors and the multiple cumulative change in function used individual development ("growth") functions of the term age times $height^2$ that best linearized the changes in lung function with time. This is the same term found to best describe the rate of change in adults in our study (18), and found previously with other descriptive methods (17). The interaction is important biologically, as explained above. For subjects with at least 3 data points, standard errors of estimate derived in the process were used as measures of individual variability in analyses of the slope using the approach of Goldstein (21, 22). In this approach, developmental ("growth rate") functions (or individual "slopes") are the dependent variables analyzed in generalized mixed linear models with covariables (age, sex, height), risk factors of
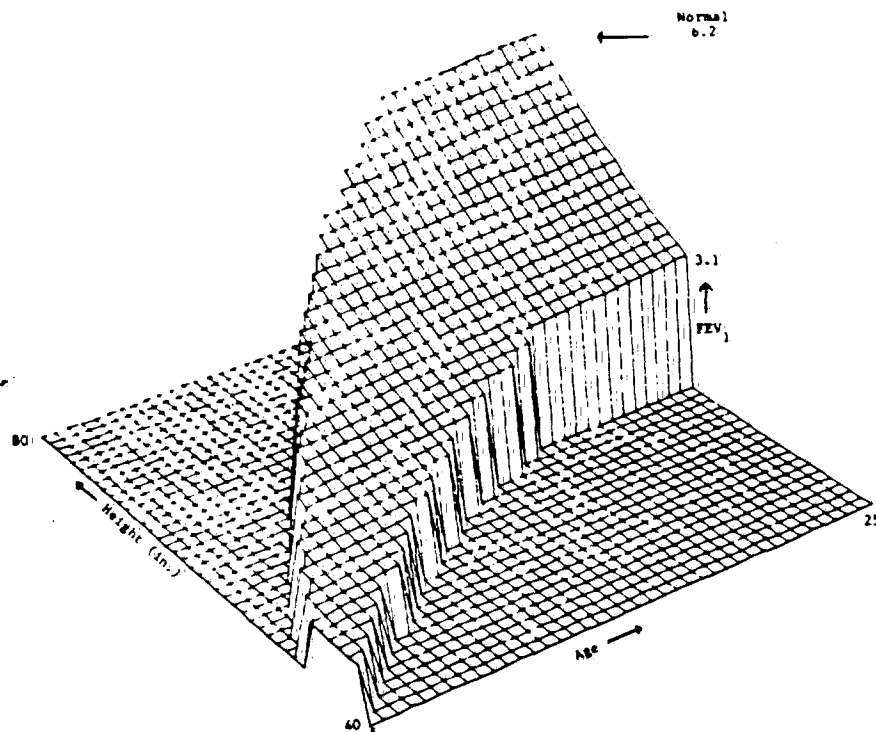
Fig. 1. Predicted FEV₁ by age and height and symptom status (details and formulas in text).

interest, individual variability (as mentioned), numbers of observations (as mentioned), and years of follow-up. Hierarchical approaches were evaluated in these processes. One can then use variables representing change (in height, smoking, etc.) as independent variables.

Personal smoking and the standard airways obstructive disease (AOD) symptoms were derived from questionnaires completed over time by the subject or by the parent when the subject was younger than 15 yr of age (12, 14-18).

Results

The three-dimensional solution of the equation for the FEV₁ is shown in figure 1. It shows clearly the curvilinear relationship of function with age and height (and curvilinearity with both together). The three-dimensional solution was of the same form for asymptomatic non-smokers ("normals") and for others. At age 25, the results for these "other" subjects shows an apparent deficit in FEV₁ of 200 to 300 ml, approximately 6% of normal function. The equation is of the same form for the 2 genders, differing only in age contribution. The only variable showing a meaningful age-sex interaction was $Vmax_{50}/FVC$. These data are shown in figure 2.

Residuals of all pulmonary function variables were significantly related to

significant AOD symptoms in all age groups; the most sensitive indicator was $Vmax_{50}$ (table 2). Those who were asymptomatic had no significant variation of residuals of lung function with age. In contrast, most symptom groups showed variability over the age range. Those with cough appear to show an increasing loss of function with age. Asthma was related to the worst lung function in each age group.

Outcome pulmonary function was evaluated by the longitudinal status of physician-confirmed disease, specifically asthma or chronic bronchitis. Longitudinal status in those who entered the study as children (initial ages zero to

14) was considered constant (always or never), new, or remitted, as seen in table 3. Ever diagnosed asthma and chronic bronchitis had prevalence rates of 6.1 and 7.3%, respectively. About 45% of those with either diagnosis had both. Those who had physician-confirmed asthma or chronic bronchitis throughout the study had significantly lower outcome FEV₁ and especially lower outcome $Vmax_{50}$ than did those in the 3 other groups; the trends in their function were not linear, and these values after 20 yr of age were still below normal. Those who developed asthma during the study had lower outcome $Vmax_{50}$ (but not FEV₁) than did those who never had asthma or remit-

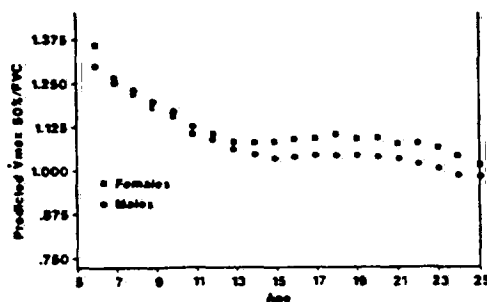Fig. 2. Predicted $Vmax_{50}/FVC$ by age and sex (details and formulas in text).

ted. Those who remitted from asthma or chronic bronchitis during the study had end-point function between those who continued to have it and those who never had it. Outcome function in different asthma histories was significantly related to age of onset (in bivariate ANOVAs only), especially $Vmax_{50}$ in those with "always asthma": mean outcome residuals were -31.2 for onsets < 5 yr and -16.0 for onsets ≥ 5 yr. As average age of new onsets was significantly different also (6.9 yr versus 3.1 yr for others), outcome $Vmax_{50}$ was adjusted for age (as seen in table 3). Sex and other factors were not significant covariates in effects of diagnosis on function.

After symptoms, smoking habits had an important effect on outcome. Residuals were significantly affected by smoking habits, both before and after adjusting for other factors (by multifactor analyses of variance). The outcomes were related to symptoms within smoking groups, as shown for FEV_1 and $Vmax_{50}$ (table 4); after adjustment for other factors, symptoms were related still to outcome $Vmax_{50}$. Sex was a significant covariable in this multivariate relationship. The interaction between smoking and symptoms was significant for both outcomes, and those who both smoked and had symptoms had the lowest end-point residuals (table 4). The number of observations per individual subject, used as a covariable, was not significant. Parental airway obstructive diseases (diagnosed emphysema, chronic bronchitis, or asthma) had additional effects with children's smoking and symptoms for end-point $Vmax_{50}$, but not independently; the residual for current smokers with symptoms and parental history was -14.41 (95% confidence interval of -4.57 to -24.25).

Parental smoking was not significant as a main effect within the multifactor analysis of variance for outcome FEV_1 or $Vmax_{50}$. However, it showed a significant interaction with subjects' smoking (children smoked if parents did) and parental AOD in its effects on $Vmax_{50}$ (table 5). There were no such associations in subjects whose parents did not have AOD (not shown). Maternal smoking is significantly related to FVC (p < 0.001), producing a positive FVC residual: $+3.13$ versus -1.48 using sex-specific equations and $+3.29$ versus -1.36 using combined gender equations. This "inverse" relationship is found in all age groups, but is significant primarily in the older age groups and in females.

For size-compensated flows ($Vmax_{50}$/FVC), females had higher predicted values between ages 13 and 25 (figure 2). Size compensation removed any further effects of age on residuals. Subjects' symptoms were still highly correlated with the outcome residuals (table 6), regardless of gender. There was a significant relationship for subjects' smoking with outcome residuals, using sex-specific or combined models. (The effect of ever smoking was seen more in those 15 to 25 yr of age at end point.) Parental smoking was not significant, though smoking habits of mothers showed a trend. (Maternal smoking was significant independently (p < 0.012) only when all observations were evaluated together.) There were no significant interactions in the multifactor ANOVA.

TABLE 2

ALL RESIDUALS OF $Vmax_{50}$ BY SYMPTOMS BY AGE GROUP*

| Ever Had Sx | All[†] | AGE (yr) | | | | Total Yes (%) |
		5.5-10	11-15	16-20	21-25	
Cough	-4.84	+0.51	-3.61	-6.34	-5.69	23.9
No	+1.43					
Phlegm	-7.20	-1.93	-10.07	-5.47	-8.42	15.8
No	+1.27					
Wheeze	-5.80	-6.68	-5.11	-5.81	-6.12	14.2
No	+2.83					
Attacks sob wheeze	-8.51	-6.22	-8.91	-10.44	-6.17	13.9
No	+1.46					
Any asthma	-13.58	-17.97	-13.95	-10.80	-15.69	7.4
No	+1.26					

* ANOVA. YES versus NO: p < 0.001 for Yes versus No
[†] The number of observations (persons times tests, for persons with 3+ tests) = 1,487.

TABLE 3

OUTCOME FEV₁ AND $Vmax_{50}$ RESIDUALS BY PHYSICIAN CONFIRMED ASTHMA: CHILDREN < 14 YEARS OF AGE

| | Number | FEV₁ | | $Vmax_{50}$ (unadjusted) | | $Vmax_{50}$ (adjusted)[†] |
		Mean	SD	Mean	SD	Mean
MD asthma						
Always	9	-6.94	11.05	-24.49	19.20	-24.8
New	24	-0.69	18.74	-16.19	20.15	-20.9
Remission	17	-0.77	16.04	-1.97	29.71	+1.37
Never	390	+3.02	13.37	+1.69	25.13	
Overall (ANOVA)		p = 0.07		p < 0.0002		p < 0.05
Any asthma outcome		-2.36	p = 0.03	-17.43	p < 0.0001	

* Adjusted values for age and asthma groups only. There were significantly different means by age of onset (< 5 versus > 5) and significantly different age of onset of new cases: 6.9 ± 5.8 versus 3.1 ± 2.7 for "always" and "remission" (p < 0.008) so means were adjusted for age by ANOVA; age of onset was not a significant main or interactive effect in overall ANOVA values. Sex was adjusted for, though not a significant covariable, because of slight differences in trends

TABLE 4

OUTCOME FEV₁ AND $Vmax_{50}$ RESIDUALS BY CHILDREN'S SMOKING AND SYMPTOMS: CHILDREN < 14 YEARS OF AGE AT ENTRY (n = 237)*

| | Smoking | | | | | | |
| Symptoms | FEV₁ | | | $Vmax_{50}$ | | | |
	Current	Ex	Never	Current	Ex	Never	Adjusted[†]
Ever	-2.77	-1.59	2.48	-12.12	-4.69	0.10	-4.33
Never	1.26	13.08	2.71	-1.90	8.93	3.66	2.43
	p < 0.02			p < 0.04			
Adjusted[†]	-1.49	8.83	2.86	-7.44	-0.04	2.85	

* Reduced N related to availability of information on all variables. All p values by ANOVA
[†] For FEV₁, adjusted for symptoms, passive smoking, parents' AOD, and age group (all ns) and sex (significant) in ANOVA p < 0.077 for adjusted smoking; significant interactions of smoking with symptoms (p = 0.044). For $Vmax_{50}$, adjusted mean effects for each other, age, sex, parents' AOD and smoking, and number of observations (all ns) in ANOVA: p <0.031 for adjusted smoking and p > 0.044 for adjusted symptoms.

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TABLE 5

OUTCOME $Vmax_{50}$ RESIDUALS BY CHILDREN'S SMOKING[*], PARENTS SMOKING, AND PARENTS' AOD[†]: CHILDREN < 14 YEARS OF AGE AT ENTRY[‡]

Smoking	Total[¶]		Parents with AOD	
	Current	Never	Current	Never
Parents' Smoking				
Mother[§]	-9.13[¥]	4.48	-9.09	2.36
Father only	-5.73	1.28	-3.23	-11.04
Father[§]	-7.07	0.71	-6.53	-7.00
Neither	-0.40	5.86	0.25	13.88
ANOVA (vs neither)	Mother[§] and father only ns.		ns	
	Father[§], p < 0.03.		< 0.06	

[*] Ex-smokers not shown.
[†] As diagnosed emphysema, chronic bronchitis, or asthma.
[‡] Ages 12.4 to 26.4 yr at end point.
[¶] Reduced N related to availability of information on all variables and age (170).
[§] Or spouse smoking.
[¥] 95% confidence interval is -1.85 to -16.41, all others encompass 0.

TABLE 6

OUTCOME $Vmax_{50}$/FVC RESIDUALS RELATED TO CHILDREN'S SMOKING AND SYMPTOMS, AND PARENTAL SMOKING (n = 389): CHILDREN < 14 YEARS OF AGE AT ENTRY

Adjusted Independent Factors[*]	Adjusted Means	p Values
Subjects symptoms		
Yes	-3.24	
No	-0.67	< 0.014
Subjects smoking		
Ever	-10.02	
Never	-1.25	< 0.013
Mothers' smoking[†]		
Current	-4.41	
Ex	-3.61	
Never	-0.40	> 0.42
Overall ANOVA		< 0.001

[*] These main effects adjusted for sex (p < 0.001), age (ns), and each other; fathers' smoking removed (as inconsistent trend).
[†] Adjusted for fathers' smoking as well.

TABLE 7

INDIVIDUAL GROWTH RATES[*] OF FEV_1 AND $Vmax_{50}$ BY RISK FACTORS,[†] COVARIABLES,[‡] AND INDIVIDUAL VARIABILITY[¶]

	Number[¥]	Adjusted FEV_1	Adjusted $Vmax_{50}$
Smoking			
Current	52	0.74	0.85
Ex	20	0.85	0.92
Never	137	0.83	0.93
		p = 0.055	p = 0.005
Symptoms			
Yes	(79)	—	0.74
No	(130)	—	0.93
		ns	p = 0.014

[*] Coefficient of (age × ht²) × 1,000.
[†] Smoking and symptoms adjusted for each other as well as the other factors (including parental smoking, which was not significant).
[‡] Age and sex (significant).
[¶] Using SEE (correlated with # tests and age, not with risk factors), and number of observations. (Correlated with age, years of follow-up, and with unadjusted FEV_1.)
[¥] Reduced because of lack of data on individual smoking (e.g., ages under 15 yr) or symptoms.

The use of the repeated measures ANOVA linear model confirmed the findings posited. Thus, residuals from the fitted developmental curves analyzed by multifactorial ANOVA/ANCOVA "fit" the more general linear model.

Results of Individual Development Model

As previously stated, individual "growth" rates ("slopes") were evaluated following the approach of Goldstein (21, 22), using multifactorial analysis of covariance. Standard errors of estimate (SEE) were used as a covariate for individual variability (within and between surveys). The SEE were significantly correlated with the number of tests and age, but not with any of the risk factors. The number of observations per individual was used as a covariable also. It was correlated with age (and, of course, years of follow-up). It was correlated significantly with unadjusted mean FEV_1 in the different surveys, though without trend, indicating random survey differences. The individual "slopes" were not correlated with initial values, but were correlated with end-point (final follow-up) values. After each explanatory variable was adjusted for covariables and other explanatory variables, only symptoms and smoking were highly related to individual slopes, especially those of $Vmax_{50}$ (table 7).

Discussion

The composite unweighted method was used to obtain the best descriptive fit for lung function development (i.e., growth) curves. It was not developed only to look for deviations/variations from time trends, as with time series models. The method used was found to be very robust. It adjusted for age and for body size (standing height), after which other measurements (sitting height, arm span) did not contribute to explaining functional measurements. Unfortunately, we did not make chest measurements, which have been found to help explain the growth curve in late adolescence and early twenties (8). The method is not intended as a reference formula. It is the mathematical best fit to the data and is not assumed to adequately describe biologic growth, although the solutions parallel our previous descriptive results (18).

The method provided very similar results for those with different numbers of observations, as long as subjects have 3 or more observations over an 8- to 12-yr period. Individuals with only 2 points do not provide sufficient information and do not fit the curvilinear solutions. Over lengthy time periods, observations on an individual subject appear to be distributed over the entire age range, thus minimizing dependency of observations. (Thus, there were no major losses of degrees of freedom or increased inter-

dependence of the observations based on the number of values used for an individual subject.) We used values that could be examined at the follow-up end point and at onset. The use of residuals was very convenient statistically in that it led to variables that were approximately normally distributed, around a zero average, and was equivalent to looking at percentages above normal and percentages below normal in evaluating other factors affecting the development curve.

The use of the repeated measures ANOVA linear model (19, 20) as an adjunct to the composite-residual method showed that the descriptive fit, used for physiologic purposes/results yielded a good fit to a general linear model. The use of ANOVA/ANCOVA to analyze differences, as per Ware and coworkers (9), was a very robust and pragmatic approach. Results that can be provided as actual decrements of function are far more understandable than are odds ratios or chi-square results.

Residuals were used to examine the phenomena of "tracking" the subjects' values over time. Thus, the relation of each one to "average" growth in this population was evaluated by looking at any change in the relation of the deviations from average (i.e., these residuals) over time. Normal subjects showed negligible mean change in their residuals from initial to end point per annum. The grand mean change in residuals was only 0.26%, even including those with symptoms, smoking, and other risk factors. Only active smoking disturbed the tracking with any significance ($p = 0.099$), with current smokers having an adjusted mean change of -0.64%. Symptoms, often present initially, only produced a -0.19% change ($p = 0.17$). Other factors had no apparent influence on tracking.

The number of observations related significantly but without pattern only to survey. In all methods of analysis, the number of observations was used as a covariate as a measure of individual variability; its lack of significant contributions was considered another indication of the strength of this approach to modeling. The SEE derived for each subject with ≥ 3 values represents a measure of within-individual variability. It was found to be unrelated to any risk variables, and related only to age and the number of observations. The SEE was used as a covariate in analyses of growth rates (individual "slopes"), using a linear model after the fashion of Goldstein (21, 22), to determine contributions of risk variables to changes over time. The results therefrom substantiated previous results, as well as providing another measure of outcome.

Size-compensated flows (expressing $V_{max_{50}}$ in FVC seconds) showed the same pattern with age and by sex (figure 2) as shown in infants and smaller children (10, 23); females had higher flows for given volumes than did males after puberty, even though males had higher volumes. For size-compensated flows, sex-specific analysis yielded the same results as those obtained for the combined group using gender as a covariable. Flows per se ($V_{max_{50}}$) did not differ significantly by gender. As discussed by us previously (10, 14-18, 23) and by others (3, 8, 11), the FEV_1 and flows do measure airway and parenchymal changes, and one can discriminate differential contributions, especially when evaluating flow as a ratio to vital capacity.

Symptomatology contributed as well to outcome function as another predictor of risk, but not to individual rates of growth. Outcome function, of course, was very well correlated with outcome symptomatology as well, and to individual growth rates. Outcomes related specifically to incidence and remission of asthma and chronic bronchitis. As shown by others (11), abnormalities of flow (i.e., the $V_{max_{50}}$) persist longer, into adulthood.

Further, children's symptomatology (by parental response and self response) was related to parental history of AOD. The latter did relate to outcome of symptomatology, and it modified effects of other factors (see below). Initial measured pulmonary function was influenced by both parental factors and the children's respiratory history, and growth in function was affected by these factors, the level of their initial function, and later symptomatology. This information confirms longitudinally, in a preliminary fashion at least, that our hypotheses that childhood respiratory trouble, effects of key respiratory illness, and the effects of parental/familial factors are all important in growth of pulmonary function in children (24-26).

Smoking had a major effect on growth of pulmonary function as well, and there was an interaction of smoking habits of the subjects and symptomatology on outcome of pulmonary function. Ex-smokers may have shown a rebound phenomenon, seen in analyses of young adults (27). Children appear to smoke in part because parents do. As found by many others, there was a significant relationship between the smoking habits of parents and those of their children, especially between those of the same gender. Likewise, mothers and fathers who smoked usually had spouses who smoked.

Further, parental smoking had an influence on the children's pulmonary function outcome. It was most evident in current smokers, symptomatic subjects, and those with a parental history of AOD. Mothers' smoking was significant, as found by others (9, 28), but we also found fathers' smoking to be important. Parental smoking did not influence height at any age, as suggested by these previous studies. We found that subjects did have increased volumes (FVC) and decreased flows if parents smoked. The effect did not differ by gender and was noted even in 5 to 7-yr-olds, although the magnitude was greater in older children and young adults. It is interesting that preliminary studies on infants (29) suggest that children of smoking mothers, especially males, may have elevated functional residual capacities even shortly after birth. We have observed also that adult male smokers who show a rapid subsequent functional decline are likely to have well-preserved FVC values at an early stage of their illness (30). The mechanism underlying these observations remains unclear, but it would appear that an increase in lung volume could be an early manifestation of the effects of active or even passive smoking, related to stimulation effects of nicotine, or growth compensatory effects related to CO exposure and/or possible loss of lung elasticity.

Our robust method of lung function growth showed effects on function of various risk factors that are highly compatible with those seen using the traditional general mixed linear model and additional linear model of individual growth (21, 22). Thus, the linear models used are consistent in this population in reflecting actual growth of pulmonary function and the factors that affect it.

In conclusion, pulmonary function growth is significantly related to children's respiratory symptoms and disease, and their smoking; parental/familial factors are important in some subgroups as well. Surprisingly, symptoms/disease are not integral in analyses in other studies (9, 28), nor are the interactions of important risk factors. The effects of parental smoking are somewhat inconsistent; in some cases a maternal smoking

effect is noted only within other risk factor subgroups. The independent and interactive effects are seen as perturbations in the growth curve as well as in outcome function (FVC, FEV_1, $Vmax_{50}$, $Vmax_{50}/FVC$). Flows ($Vmax_{50}$) and size-compensated flows ($Vmax_{50}/FVC$) were the most sensitive, and often showed persistence of decrement related to early events.

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The authors of this study investigated parental smoking habits, pulmonary function capabilities, and nonspecific bronchial responsiveness to eucapneic hyperpnea with subfreezing air in a community-based sample of children and young adults.

The Effect of Passive Smoking on Pulmonary Function and Nonspecific Bronchial Responsiveness in a Population-based Sample of Children and Young Adults[1-4]

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Introduction

Recent scientific investigations have observed adverse effects of parental cigarette smoking on level of pulmonary function (1) and rate of change of pulmonary function (2) in children. Whether passive smoking is an independent risk factor for these outcomes in children or whether the effects of passive smoking result from associations with other putative risk factors, such as respiratory infections (3, 4) or the occurrence of the atopic state (5), remains unclear. The association of parental cigarette smoking with wheezing symptoms in children (6, 7) as well as the identification of parental smoking as a factor that exacerbates the symptoms of childhood asthma (8) suggests a potential relationship between passive cigarette smoking and nonspecific bronchial responsiveness. To investigate this possibility, we studied parental cigarette smoking, pulmonary function, and nonspecific bronchial responsiveness to eucapneic hyperpnea with subfreezing air in a community-based sample of children and young adults.

Methods

Population

Details of the initial selection of the study population have been published previously (1). A random sample was selected from all children 5 to 9 yr of age in the public and parochial school systems of East Boston as of September 1974. These index children along with all members of their households constituted the initial study population. All members of the cohort have been screened on an annual basis since 1975, except for the second and third years when only index children were studied. Standardized questionnaires have been used to obtain information on respiratory symptoms and illnesses, smoking history, and demographic data. Parents answered for children 10 yr of age and younger, except for questions about the child's smoking history, which were asked during pulmonary function testing when the parents were not present. Asthma was defined as an affirmative response to a question about whether the subject has been told he or she has asthma by a doctor within the past 12 months. "Any wheeze" was defined as any category of affirmative response to a question about wheezing within the past 12 months. Episodes of dyspnea and wheeze were considered present if there was an affirmative response to a question about the occurrence of such episodes within the past 12 months. Current cigarette smoking was defined as currently smoking at least 1 cigarette per day or having quit such a habit within the past 12 months.

Pulmonary Function Testing

Subjects performed FVC maneuvers with the use of an 8-L, water-filled, portable, recording spirometer (Survey Spirometer; Warren Collins, Braintree, MA) while in the sitting position and without the use of noseclips; FVC, FEV_1, and FEF_{25-75} were measured using standard techniques. Mean values for the best of 3 of 5 acceptable tracings were used for analysis. All values were corrected to BTPS.

Cold Air Protocol

During the sixth through eighth interview cycles (1980 to 1982), a sample of the cohort families was selected to participate in a study of bronchial responsiveness to eucapneic hyperpnea with subfreezing air and allergy skin testing. An attempt was made to include as many subjects as possible who reported a history of asthma or wheezing, but asymptomatic subjects were selected randomly. If possible, the protocol was not performed within 3 wk of a respiratory infection, but this was not always achieved in the winter. After completing the questionnaire and spirometry as described above, subjects performed eucapneic hyperpnea with subfreezing air using the technique of Deal and coworkers (9). Subjects hyperventilated with cold air for 4 min with a target minute ventilation of 25 times the initial FEV_1. Five minutes after completing cold air hyperpnea, repeat spirometry was performed. After completing the above protocol, each subject underwent allergy skin testing by the prick method. Four common environmental antigens were tested: mixed trees, mixed grasses, ragweed, and house dust. Atopy was defined as the occurrence of any wheal for at least one antigen.

Data Analysis

Response to cold air was evaluated by taking the difference between the prechallenge and postchallenge FEV_1 (ΔFEV_1). To correct for size, 2 analytic methods were employed. One method consisted of dividing ΔFEV_1 by predicted FEV_1 calculated from standard regression equations (10). Using predicted FEV_1 for this purpose offered several advantages. Predicted FEV_1 had a slightly higher correlation with ΔFEV_1 ($r = 0.36$) than did height ($r = 0.31$) or height^3 ($r = 0.33$). Use of predicted FEV_1 avoided size-correcting by a measure that itself may reflect bronchial tone, such as FVC or FEV_1. Finally, ΔFEV_1 as a percent of predicted FEV_1 is easily interpreted. The other method of size correction employed a linear regression model with ΔFEV_1 as the dependent variable and predicted FEV_1 along with exposure as the independent variables.

Chi-square test, t tests for independent samples, multiple linear regression, and stepwise

TABLE 1

SUBJECTS STUDIED WITH AIR COMPARED WITH OTHER SUBJECTS
IN THE POPULATION SAMPLE

	Subjects Year 6, 7, or 8 with Cold Air Data	Number	Subjects Year 6, 7, or 8 Without Cold Air Data	Number
Age, yr*	12.8 ± 0.2	292	12.9 ± 0.1	586
Current asthma, %	7.2†	292	3.9†	586
Any wheeze, %	18.9‡	291	12.3‡	586
Current personal smoking, %	7.9†	280	13.8†	552
Current maternal smoking, %	61.9	286	56.9	576
Current paternal smoking, %	43.1	274	48.2	562
FVC., % pred*	101.3 ± 0.8	292	100.8 ± 0.7	409
FEV., % pred*	103.7 ± 0.8§	292	106.5 ± 0.8§	426
FEF₂₅₋₇₅, % pred*	92.6 ± 1.3§	292	97.4 ± 1.1§	409

* Values are mean ± SE.
† p < 0.05 by chi-square.
‡ p < 0.01 by chi-square.
§ p < 0.02 by t test for independent samples.

linear regression were performed using the Statistical Analysis System, Inc. software package (11). In regression models, discrete variables were assigned values of zero or 1 as follows: sex (1 = male), current personal smoking (1 = smoker), current maternal smoking (1 = smoking mother), current paternal smoking (1 = smoking father), atopy (1 = atopic), and history of cold within 2 wk (1 = yes). In the stepwise linear regression procedure a significance level of 0.15 was used for entry into and retention in the model, but statistical significance was considered to be present only for p values less than 0.05.

Results

Cold air challenge was performed by 292 subjects 6 to 21 yr of age during the study period. Characteristics of these subjects and the 586 similar-aged subjects not selected for the cold air protocol are given in table 1. By design, the prevalence of current asthma was greater among cold air subjects than among those not selected for cold air (7.2% versus 3.9%, respectively, p < 0.05). The FEV₁ percent predicted and FEF₂₅₋₇₅ percent predicted were significantly lower in the cold air group, reflecting the preferential selection for the cold air protocol of subjects reporting wheeze. Personal smoking was significantly less common among cold air subjects than among subjects not chosen for cold air. Current maternal and paternal smoking did not differ significantly between the cold air group and the remainder of the population sample.

Wheezing symptoms reported by cold air subjects are given in table 2 for the 291 subjects with complete respiratory symptom data. Any wheeze and episodes of dyspnea and wheeze were reported by 14.1 and 3.0%, respectively, of subjects who denied current doctor-diagnosed asthma. Nineteen of the subjects denying current asthma had a history of previous doctor-diagnosed asthma. Current maternal smoking data were not available for 6 nonasthmatic subjects who underwent the cold air protocol, so these subjects were excluded from further analysis. Current paternal smoking data were

available for 273 of the 286 subjects included in the analysis, including 20 of the 21 asthmatic subjects.

The characteristics of the subjects who underwent cold air challenge, stratified according to current asthma and current maternal smoking status, are given in table 3. Among the 265 subjects who denied current asthma, there were no differences between maternal smoking groups with respect to age, sex, or history of a cold within 2 wk. Among the 21 subjects with current asthma, children of smoking mothers had a lower mean age, were more often male, and had a higher frequency of recent colds, but these differences were not significant. Among nonasthmatics, children of smoking mothers were significantly more likely to smoke themselves than were children of nonsmoking mothers. None of the asthmatic subjects smoked themselves. Among nonasthmatics, atopy was significantly more common among children of smoking mothers than among those of nonsmoking mothers (p = 0.02). Among asthmatics, there was a similar trend.

Nonasthmatic subjects with smoking mothers had significantly lower mean percent predicted FEV₁ and FEF₂₅₋₇₅ than did nonasthmatic subjects whose mothers denied smoking (table 3). Adjustment for personal smoking status using multiple regression did not alter the significant association between maternal smoking and low FEV₁ and FEF₂₅₋₇₅ (results not shown). Among the asthmatic subjects, those with smoking mothers had lower mean FEV₁ and

TABLE 2

SYMPTOMS REPORTED BY COLD
AIR SUBJECTS

	Subjects Denying Asthma (n)	Subjects Denying Asthma (%)	Subjects Reporting Asthma (n)	Subjects Reporting Asthma (%)
Subjects	270		21	
Any wheeze	38	14.1	17	81.0
Episodes of dyspnea and wheeze	8	3.0	10	47.6

TABLE 3

SUBJECT CHARACTERISTICS

	Nonasthmatics Nonsmoking Mother	Nonasthmatics Smoking Mother	Asthmatics* Nonsmoking Mother	Asthmatics* Smoking Mother
Subjects, n	97	168	12	9
Age, yr†	12.8 ± 0.3	12.9 ± 0.2	12.7 ± 0.9	11.0 ± 0.9
Males, %	51.5	49.4	50.0	77.8
Current smokers, %	3.1‡	11.3‡	0	0
≥ 1 possible allergy skin test, %	14.7‡ (n = 95)	27.2‡ (n = 162)	25.0	33.3
Cold within 2 wk, %	25.3 (n = 95)	25.3 (n = 166)	8.3	33.3
FVC, % pred†	102.8 ± 1.3§	99.7 ± 1.1§	104.0 ± 2.9	107.8 ± 3.8
FEV., % pred†	106.0 ± 1.4ǁ	101.4 ± 1.1ǁ	102.9 ± 3.5	100.8 ± 6.3
FEF₂₅₋₇₅, % pred† Mean ± SE	103.0 ± 2.3ǁ	88.2 ± 1.5ǁ	85.8 ± 6.8	76.1 ± 10.4

* None of the differences between maternal smoking groups are statistically significant for asthmatics.
† Values are mean ± SE.
‡ p = 0.02 by chi-square for difference between maternal smoking groups.
§ 0.05 < p < 0.10 for difference between maternal smoking groups.
ǁ p < 0.001 for difference between maternal smoking groups.

TABLE 4

**COLD AIR RESPONSIVENESS BY ASTHMA AND CURRENT
MATERNAL SMOKING STATUS**

Current Asthma Status	Current Maternal Smoking Status	Number	$\frac{\Delta FEV_1}{Pred.\ FEV_1} \times 100^*$
Nonasthmatic	Nonsmoker	97	$6.29 \pm 0.67\dagger$
	Smoker	168	$5.82 \pm 0.43\dagger$
Asthmatic	Nonsmoker	12	$11.9 \pm 4.8\ddagger$
	Smoker	9	$24.0 \pm 3.3\ddagger$

* Values are mean ± SE.
† p = 0.54 for difference between maternal smoking categories.
‡ p = 0.07 for difference between maternal smoking categories.

TABLE 5

**COLD AIR RESPONSIVENESS BY ASTHMA AND CURRENT
PATERNAL SMOKING STATUS**

Current Asthma Status	Current Paternal Smoking Status	Number	$\frac{\Delta FEV_1}{Pred.\ FEV_1} \times 100^*$
Nonasthmatic	Nonsmoker	147	$6.35 \pm 0.52\dagger$
	Smoker	106	$5.46 \pm 0.58\dagger$
Asthmatic	Nonsmoker	11	$17.1 \pm 5.7\dagger$
	Smoker	9	$15.0 \pm 3.9\dagger$

* Values are mean ± SE.
† p < 0.25 for difference between paternal smoking categories.

TABLE 6

**MULTIPLE LINEAR REGRESSION RESULTS
DEPENDENT VARIABLE: CHANGE IN FEV₁ CAUSED BY HYPERNEA WITH COLD AIR**

Group	Number	R²	Independent Variable	Regression Coefficient	Standard Error	p Value
Nonasthmatics	265	0.15	Predicted FEV₁	0.079	0.011	0.0001
			Maternal smoking	-0.011	0.021	0.62
Asthmatics	21	0.71	Predicted FEV₁	0.515	0.079	0.0001
			Maternal smoking	0.319	0.125	0.02

TABLE 7

**PULMONARY FUNCTION AND COLD AIR RESPONSE OF SUBJECTS
DENYING ASTHMA AND WHEEZE**

	Nonsmoking Mother	Smoking Mother
Subjects, n	87	139
FVC, % pred*	102.8 ± 1.4	100.9 ± 1.2
FEV₁, % pred*	$106.1 \pm 1.5\dagger$	$103.0 \pm 1.1\dagger$
FEF$_{25-75}$, % pred*	$103.9 \pm 2.4\dagger$	$90.0 \pm 1.5\dagger$
ΔFEV₁ × 100/predicted FEV₁*	6.31 ± 0.69	5.55 ± 0.47

* Values are mean ± SE.
† p < 0.01 for difference between maternal smoking groups.

FEF$_{25-75}$ and higher mean FVC than did those with nonsmoking mothers, although these differences were not significant.

Among nonasthmatics, mean cold air response expressed as ΔFEV₁ divided by predicted FEV₁, did not differ between subjects with smoking and nonsmoking mothers (table 4). Among the 21 asthmatics there was a trend toward greater cold air response in subjects with smoking mothers than in those with nonsmoking mothers (p = 0.07). Cold air response was not significantly related to paternal smoking status for either nonasthmatics or asthmatics (table 5).

Using linear regression to adjust for predicted FEV₁, the regression coefficient for maternal smoking as a predictor of ΔFEV₁, did not differ significantly from zero among nonasthmatic subjects (table 6). For asthmatic subjects, the regression coefficient for maternal smoking was significantly different from zero (p

= 0.02), indicating a significant relationship between maternal smoking and cold air response in this regression model.

Because of the possibility that some of the subjects who reported wheeze but denied doctor-diagnosed asthma may actually have had mild asthma that had not prompted them to seek medical attention, an analysis restricted to subjects who denied both asthma and wheeze was performed. As indicated in table 7, results were similar to those for all subjects denying asthma, i.e., maternal smoking was associated with significantly lower FEV₁ and FEF$_{25-75}$ but not with any alteration of cold air response.

Stepwise multiple linear regression was performed to assess the relationship between cold air responsiveness and a number of variables of potential importance. Change in FEV₁ was used as the dependent variable. Predicted FEV₁ was entered as the first independent variable to correct for size. Other independent variables analyzed were age, sex, height, current personal smoking status, current maternal smoking status, current paternal smoking status, atopy, and history of a cold in the 2 wk prior to testing. Among nonasthmatics, no variable entered the model with a regression coefficient significantly different from zero after predicted FEV₁ was entered. Among the 21 asthmatic subjects, only current maternal smoking status entered the regression after predicted FEV₁. Current maternal smoking status remained a significant predictor of ΔFEV₁, and its regression coefficient changed only slightly when adjustment for history of a cold in the previous 2 wk was accomplished by forcing this variable into the model.

Discussion

Passive smoking by children of cigarette smokers has been found to be associated with decreased level of pulmonary function (1, 6, 12–15) although several studies have observed no effect of parental smoking on spirometric values (16–18). A longitudinal study of children and young adults observed a decreased rate of change of pulmonary function among subjects with smoking mothers (2), suggesting that passive smoking may have a deleterious effect on growth of the respiratory system. The mechanisms by which passive smoking may decrease the level or rate of change of pulmonary function have not been established.

A link between cigarette smoke exposure and increased bronchial respon-

siveness has been suggested by a number of physiologic investigations of adult subjects, although the relevance of these data to passive smoking in children is not certain. Active cigarette smoking has been shown to cause an acute increase in airway resistance in normal volunteers exposed in the laboratory (19, 20). A number of investigators have examined the influence of chronic cigarette smoking on bronchial responsiveness (21-28), and most (22-28) have found greater responsiveness among smokers than among nonsmokers.

The acute effects of passive smoking in adults have been studied in the laboratory with conflicting results. Dahms and coworkers (29) observed that asthmatic subjects, but not normal subjects, experienced a decline in pulmonary function after 1 h of exposure to sidestream cigarette smoke. Wiedemann and coworkers (30) and Shephard and colleagues (31), on the other hand, found that passive smoking caused no acute change in the pulmonary function of asthmatic subjects exposed in environmental chambers for 1 and 2 h, respectively. Wiedemann and coworkers (30) measured nonspecific bronchial reactivity to methacholine 1 day before and immediately after passive smoking in these same asthmatic subjects. They observed a small but significant decrease in responsiveness after passive smoking. Interpretation of these studies is difficult since the effects of autonomic nervous system responses to the stress of the in-chamber exposure were not taken into account. Furthermore, acute exposure studies may have little relevance to the effects of chronic exposure.

Population-based studies have provided conflicting evidence regarding the influence of passive smoking on nonspecific bronchial responsiveness and asthma among children. Dodge (7) found an association between parental smoking and symptoms of cough, phlegm, and wheeze among 676 Arizona school children 8 to 12 yr of age, although parental smoking was not related to level of pulmonary function. Weiss and coworkers (6) studied 650 children 5 to 9 yr of age in East Boston and found that parental cigarette smoking was associated with the report of persistant wheeze. Gortmaker and colleagues (32) analyzed data of 3,072 children between infancy and 17 yr of age from a random household health survey carried out in Michigan and Massachusetts. The diagnosis of asthma, based on reporting by the mother, was

significantly more frequent among children with smoking mothers than among those whose mothers denied smoking. The investigators calculated that 18 to 34% of childhood asthma in their sample could be attributed to maternal smoking; however, the possibility of reporting bias in this study cannot be excluded. In contrast, Schenker and associates (3) studied 4,071 children 5 to 14 yr of age in rural Pennsylvania and found no association between parental smoking and either persistant wheeze or doctor-diagnosed asthma, although parental smoking was related to the occurrence of chest illnesses. Schilling and coworkers (17) found no association between parental smoking and respiratory symptoms among 816 children 7 yr of age and older in Connecticut and South Carolina.

In the present study, current maternal smoking was associated with significantly lower FEV_1 and FEF_{25-75} among the 265 subjects who denied recent doctor-diagnosed asthma. The magnitude of this effect was greater than that observed among our entire population (1, 6) and also exceeded that reported by other investigators who have observed significant effects of parental smoking on spirometric values (12-15). The preferential selection for cold air challenge of subjects reporting wheeze may have resulted in a sample displaying increased susceptibility to the effect of passive smoking on spirometric values, even among subjects denying recent asthma. A subject's report of recent medical therapy for asthma has been found to be a useful indicator of this disease (33), but there remains the possibility that some of the subjects who denied asthma actually had mild asthma that had not prompted them to seek medical attention. To eliminate potential error caused by misclassification of mild asthmatics as nonasthmatics, we performed an analysis restricted to subjects denying both asthma and wheeze and found results similar to those for all subjects denying asthma.

Despite the relationship between maternal smoking and pulmonary function, there was no association between maternal smoking and cold air responsiveness among subjects denying asthma. These findings suggest that decreased pulmonary function associated with passive smoking is not due to increased nonspecific bronchial responsiveness. Instead, passive smoking may alter the growth of the immature respiratory system.

If any relationship between passive smoking and nonspecific bronchial responsiveness does exist among nonasthmatic children and young adults, its demonstration may require more precise quantitation of passive smoke exposure. Household smoking reported on questionnaires correlates well with urinary cotinine as an indicator of passive smoke exposure (34, 35), but a more quantitative estimate of exposure based on cotinine measurements or detailed environmental data could enhance the investigation of passive smoking effects. In addition, cold air challenge testing, which employs a single-dose stimulus and which measures response in terms of maximal expiratory spirometric values, may not be sufficiently sensitive to detect subtle physiologic changes induced by passive smoking among the nonasthmatic population. Other physiologic techniques, such as bronchial provocation tests employing incremental doses of bronchoconstricting stimuli or partial expiratory flow-volume measurements, might improve sensitivity to such changes.

An important self-selection process also may serve to mask a relationship between passive smoking and bronchial responsiveness. Persons who are genetically predisposed to higher levels of bronchial responsiveness may tend to avoid smoking or to quit smoking once they start, whereas those who start and continue to smoke may be relatively less predisposed to the development of hyperresponsiveness. Because of this 'healthy smoker effect,' smoking families may be genetically inclined to lower responsiveness than nonsmoking families, obscuring any increase in bronchial responsiveness caused by active or passive cigarette smoking. This may explain the lower prevalence of maternal smoking among asthmatic subjects than among nonasthmatic subjects in the present data. Studies using longitudinal designs beginning in early childhood would be better able to shed light on these interrelationships, since bronchial responsiveness measured early in life could serve as a baseline, with subsequent examinations reflecting the effects of exposure. Cross-sectional data, such as presented in this report, should be interpreted with caution.

Among the 21 asthmatic subjects in the sample, maternal smoking was associated with higher mean FVC and lower mean FEV_1 and FEF_{25-75}, but these differences were not significant. Cold air responsiveness was greater among subjects with smoking mothers than among those with

nonsmoking mothers. Expressed as a percent of predicted FEV_1, the change in FEV_1 caused by eucapneic hyperpnea with subfreezing air was approximately twice as high among asthmatic children of smoking mothers as among those of nonsmoking mothers, a difference that was not significant ($p = 0.07$). In the linear regression analysis, maternal smoking was a significant ($p = 0.02$) predictor of ΔFEV_1 after adjusting for predicted FEV_1. In stepwise linear regression using change in FEV_1 as the dependent variable and predicted FEV_1 as the first independent variable, maternal smoking status was the only other independent variable that entered the model for the asthmatic subjects. The lack of a similar relationship between cold air response and paternal smoking may reflect less time spent at home or in close proximity to the children by fathers than by mothers.

Because our population-based sample contained a relatively small number of asthmatics, findings regarding the effects of passive smoking on young asthmatics should not be considered conclusive. Our data are in agreement with those of Murray and Morrison (36), who observed greater nonspecific bronchial responsiveness to histamine in association with maternal smoking among 94 asthmatic children. These data provide a physiologic basis for the retrospective findings of O'Connell and Logan (8), who reviewed the records of 400 asthmatics and found that parental smoking frequently exacerbated asthma symptoms, which often improved when parents stopped smoking.

In conclusion, among the 21 asthmatic children and young adults in this population-based sample, there was a relationship between bronchial responsiveness to cold air and that was of borderline significance. We were unable to demonstrate any effect of parental smoking on bronchial responsiveness among 265 similar-aged nonasthmatic subjects, despite the occurrence of significantly lower levels of FEV_1 and FEF_{25-75} in association with maternal smoking. These findings suggest that lower levels of childhood pulmonary function associated with maternal smoking may not be due to increased bronchial responsiveness. Further research using more precise quantification of exposure and more comprehensive physiologic evaluation may help elucidate the effects of passive smoking during growth of the respiratory system.

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ABSTRACT. Previous studies have suggested that passive smoking (involuntary inhalation of tobacco smoke by nonsmokers) reduces small airways function. We evaluated the exposure to passive smoking and its effects on pulmonary function and symptoms in a group of 12- to 17-year-old high school athletes (N=209; 119 boys and 90 girls) at their annual presport participation physical examinations. A structured interview was used to assess pulmonary symptoms, personal smoking habits, and passive cigarette smoke exposure. All athletes performed forced expiratory maneuvers on a portable spirometer. We measured forced vital capacity, forced expiratory volume in 1 second, and forced expiratory flow 25% to 75% (FEF25-75). The best of three FEF25-75 measured was used. Less than 70% of predicted FEF25-75 was considered abnormal. Of the 209 athletes, 7.7% were active smokers and were excluded. Of the remaining 193 athletes, 68.4% were currently exposed to passive smoking. We found a fourfold increase in incidence of low FEF25-75 and/or cough in athletes exposed to passive smoking compared with athletes not exposed: 18 of 132 exposed athletes (13.6%) had low FEF25-75 and/or cough compared with two of 61 unexposed athletes (3.3%) who had low FEF25-75 and cough (P=.02). Boys were more frequently exposed to passive smoking than girls (74% of boys [80/108] v 61% of girls [52.85]), but the effects were more pronounced in girls. These data show a relationship between exposure to passive smoking and early pulmonary dysfunction in young athletes. The frequent exposure to passive smoke and the high prevalence of dysfunction in this population, generally considered to be healthy, is of particular concern.

Reduction in Pulmonary Function and Increased Frequency of Cough Associated With Passive Smoking in Teenage Athletes

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ABSTRACT. Previous studies have suggested that passive smoking (involuntary inhalation of tobacco smoke by nonsmokers) reduces small airways function. We evaluated the exposure to passive smoking and its effects on pulmonary function and symptoms in a group of 12- to 17-year-old high school athletes (N = 209; 119 boys and 90 girls) at their annual presport participation physical examinations. A structured interview was used to assess pulmonary symptoms, personal smoking habits, and passive cigarette smoke exposure. All athletes performed forced expiratory maneuvers on a portable spirometer. We measured forced vital capacity, forced expiratory volume in 1 second, and forced expiratory flow 25% to 75% (FEF_{25-75}). The best of three FEF_{25-75} measured was used. Less than 70% of predicted FEF_{25-75} was considered abnormal. Of the 209 athletes, 7.7% were active smokers and were excluded. Of the remaining 193 athletes, 68.4% were currently exposed to passive smoking. We found a fourfold increase in incidence of low FEF_{25-75} and/or cough in athletes exposed to passive smoking compared with athletes not exposed: 18 of 132 exposed athletes (13.6%) had low FEF_{25-75} and/or cough, compared with two of 61 unexposed athletes (3.3%) who had low FEF_{25-75} and cough ($P = .02$). Boys were more frequently exposed to passive smoking than girls (74% of boys [80/108] v 61% of girls [52/85]), but the effects were more pronounced in girls. These data show a relationship between exposure to passive smoking and early pulmonary dysfunction in young athletes. The frequent exposure to passive smoke and the high prevalence of dysfunction in this population, generally considered to be healthy, is of particular concern. Pediatrics 1987;80:32-36; passive smoking, cough, spirometry, adolescent, athlete.

Passive smoking, or involuntary inhalation of tobacco smoke by a nonsmoker, has been implicated as a threat to health.[1-4] Sidestream smoke arising from the burning end of a cigarette produces approximately two thirds of the air pollution resulting from tobacco smoke in a room.[5] Concentrations of most toxins and carcinogens present in cigarette smoke are higher in sidestream than in exhaled mainstream smoke.[6] Reports of adverse health effects from passive smoking range from increased frequencies of acute and chronic respiratory illnesses in infants and young children to a higher incidence of lung cancer in nonsmoking spouses.[7-14] Recent studies have shown an overall increased cancer risk in passive smokers, with the greatest risk being in adults who have been passive smokers since childhood.[15,16]

In studies of young children, exposure to parental smoking has been associated with a greater frequency of respiratory symptoms such as cough, increased mucous production, and wheezing, as well as an increased incidence of asthma and bronchiolitis.[8,13,14,17] Impaired pulmonary function has been observed in nonsmoking children whose parents smoke, suggesting a reduction of small airways function due to passive smoking early in life.[18-20]

In this study, we evaluated the effects of passive smoking exposure on pulmonary function and

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symptoms in a group of high school athletes. We defined passive smoking exposure as living at home with one or more smokers or being exposed to a friend's cigarette smoke for at least two hours per week.

MATERIALS AND METHODS

In August 1985, during a five-day period, we performed physical examinations on approximately 600 teenage athletes 12 to 17 years of age at five suburban high schools in Nassau County, New York. Because of time constraints in completing the standardized questionnaires and performing pulmonary function testing, we limited the number of athletes sampled to no more than 45 per day. Boys or girls were sampled on alternate days, starting with boys on the first day. A structured interview assessing personal tobacco use, passive smoking exposure, and pulmonary symptoms was given by one of us (M.S.J.). Histories of smoking by all household members and peers were obtained from the athletes. No athlete was currently receiving medication, but several reported a medical diagnosis of a pulmonary condition. Subjects were specifically asked about symptoms of cough, wheezing, or dyspnea during exercise or at rest. Data were analyzed using χ^2 analysis or Fisher exact test. Relative risk is the ratio of the prevalence of abnormal findings in the exposed to unexposed groups.

After the questionnaires and standard physical examinations were completed, the athletes performed forced expiratory maneuvers on a portable spirometer (Devilbiss Surveyor I, Somerset, PA). Daily verification of calibration was done using a precalibrated 3-1 Devilbiss surveyor syringe. We measured forced vital capacity, forced expiratory volume in 1 second, and forced expiratory flow at 25% to 75% of vital capacity (FEF_{25-75}). Studies have shown that FEF_{25-75}, which corresponds to expiratory flow when 25% to 75% of forced vital capacity is expired, is the most sensitive of the common spirometric indicators of small airways dysfunction.[21] Less than 70% of predicted FEF_{25-75}, which corresponded to the lower fifth percentile in our study, was considered abnormal. Our intention was to consider the lower 5% of FEF_{25-75} values as

abnormal because that level is used extensively as a criteria of an abnormality. All pulmonary function measurements were expressed as percentages of predicted values for age, height, weight, sex, and race using nomograms of Polgar and Promadhat[22] and Knudson et al.[23] The best of three acceptable FEF_{25-75} measures was used for data analysis, allowing a maximum of 5% difference between tests.

RESULTS

A total of 209 athletes were asked and agreed to complete the questionnaire and to undergo pulmonary function testing. Of these, 16 (7.7%) were active smokers or exsmokers and were excluded. Three of the 16 active smokers (19%) had abnormal FEF_{25-75} values and/or cough. Of the remaining 193 nonsmoking athletes, 132 (68.4%) were currently exposed to passive smoking. The specific sources of passive smoke exposure are shown, in descending order, in Table 1. It is evident that exposure to smoking parents accounted for the majority of exposure, but friends also provided a sizeable source of exposure, either alone or in combination with other family members. The characteristics of the currently exposed and unexposed groups of teenage athletes are given in Table 2. The two groups were similar except for sex; 61% of boys were in the exposed group v 47% of girls ($P = .04$). The sample size was inadequate to allow grouping of exposure in a way that would permit evaluation of dose-response relationships.

The reported frequency of respiratory conditions and symptoms for both groups is given in Table 3. The frequency of allergies, asthma, bronchitis, shortness of breath, and wheezing was similar in the exposed and unexposed athletes. The frequency

TABLE 1. Sources of Passive Smoke Exposure

Source of Exposure	% of Adolescents
Mother or father	23.5
Mother and father	18.2
Mother or father and friends	14.4
Friends only	11.4
Mother, father, and siblings	6.8
Siblings only	3.0
Other combination of above	22.7

TABLE 2. Characteristics of Currently Exposed and Unexposed Teenage Athletes

Characteristic	Unexposed Athletes (n = 61)	Exposed Athletes (n = 132)
Age (mean yr ± SD)	15.0 ± 1.7	14.7 ± 1.7
Height (mean cm [in] ± SD)	166.1 ± 10.4 [65.4 ± 4.1]	166.4 ± 10.2 [65.5 ± 4.0]
Wt (mean kg [lb] ± SD)	59.0 ± 13.1 [131.1 ± 29.0]	60.8 ± 13.5 [135.0 ± 30.0]
Race (% white)	78.3	88.5
Sex (% boys)	46.7	60.7

TABLE 3. Respiratory Conditions and Symptoms by History

Condition or Symptom	% of Athletes Exposed to Passive Smoking	% of Athletes Unexposed to Passive Smoking
Allergies	10.0	15.5
Asthma	6.9	6.9
Bronchitis	2.3	5.2
Shortness of breath	5.8	7.1
Wheeze	3.1	3.4
Cough	7.2	1.8

TABLE 4. Athletes with Abnormal Forced Expiratory Flow 25% to 75% (FEF_{25-75})

FEF_{25-75} Value	% of Athletes Exposed to Passive Smoking (n = 132)	% of Athletes Unexposed to Passive Smoking (n = 61)
>70%	92.4	96.7
<70%	7.6	3.3

of cough was four times greater in the group exposed to passive smoking ($P = .08$). The frequency of abnormal FEF_{25-75} values in the exposed and unexposed groups is shown in Table 4. Among exposed athletes, 7.6% had a low FEF_{25-75} value, whereas among unexposed athletes, 3.3% had a low FEF_{25-75} value. This was a 2.3-fold increase in frequency of low FEF_{25-75} values in athletes currently exposed to passive smoking ($P = .21$).

Although cough and abnormal FEF_{25-75} values were each higher in frequency in the exposed than in the nonexposed athletes, the differences, when considered separately, were not statistically significant. When cough and low FEF_{25-75} value were combined, as shown in Table 5, the percentage of athletes with abnormal FEF_{25-75} values and/or a history of cough was 13.6% of the exposed subjects v 3.3% of the unexposed athletes, this being a fourfold increase in the frequency of these conditions in exposed athletes, which is a statistically significant difference ($P = .02$). The association between exposure to passive smoking and abnormal FEF_{25-75} value and/or cough was statistically significant for girls ($P = .03$). For boys, the relationship was consistent but not significant ($P = .29$) (Table 5).

DISCUSSION

The data in this study show a relationship between passive smoking and early pulmonary dysfunction and symptoms in young athletes. The high prevalence of passive smoking exposure in this group of athletes who had never smoked (68%) is comparable with other reports.[1,20] Earlier findings reported by Tager and associates,[18,19] although lacking quantitative measurements of passive smoking exposure, showed that cigarette smoking by parents

had a measurable effect on decreased pulmonary function in the children independent of any direct use of cigarettes by the children. In their longitudinal study,[19] they showed that the lungs of nonsmoking children whose mothers smoked grew at only 93% of the rate of growth in nonsmoking children with nonsmoking mothers. In adolescence, peers become an increasingly important contributing factor to passive smoking exposure, sometimes being the only source of this exposure, as it was for 11.4% of athletes in this study. A recent study of the effect of passive smoking on children's pulmonary function in Shanghai[24] showed a decrease in pulmonary function that was related to the father's cigarette smoking. All of the mothers denied smoking in that study, and passive smoking exposure from peers was not investigated, an important consideration because 8- to 16-year-old subjects were studied. Nevertheless, the Shanghai study's finding that the effect of passive smoking is greater in school girls than boys was repeated in the present study.

Charlton[13] has shown a link between parental smoking at home and the reporting of frequent coughs by children 8 to 19 years old who had never smoked. Frequent coughs may indicate acute and chronic pulmonary irritation or pathology—a possible result of respiratory tract damage from passive smoking. In this study, we noted a fourfold increase in report of coughs by the athletes exposed to passive smoking. Charlton, surveying 15,709 athletes, showed a dose-response effect of parental smoking on cough, with increasing likelihood of cough being reported depending on whether none, one, or both parents smoked.

When the same investigators question and test subjects, the possibility of interview bias is raised. In this study, the investigators who performed the pulmonary function testing were blinded to questionnaire results. Another possible source of bias is in the child's report of parental smoking. The validity of the self-report method has been verified by Jarvis and associates,[25] who used salivary cotinine levels as a biologic marker of passive smoke exposure in children. Cotinine, a major metabolite of nicotine that is specific to tobacco smoke, appears

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TABLE 5. Athletes With Abnormal Forced Expiratory Flow 25% to 75% (FEF_{25-75}) or Cough by Exposure to Passive Smoking

FEF_{25-75} Value	Both Sexes*		Girls†		Boys‡	
	Exposed	Unexposed	Exposed	Unexposed	Exposed	Unexposed
>70% without cough	114	59	45	32	69	26
<70% or cough	18	2	7	0	11	2

* FEF <70% or cough among exposed (13.6%) v unexposed (3.3%); relative risk = 4.1, $P = .02$.

† $P = .03$.

‡ $P = .29$.

to be the marker of choice for quantifying passive exposure to cigarette smoke.[26,27] Jarvis et al found that average concentrations of cotinine in saliva increased in a dose-related fashion; the more sources of exposure the child reported, the higher the level of cotinine in his or her saliva.

CONCLUSION

Our study results are consistent with previous studies showing a relationship between passive smoking and increased frequency of cough and decreased pulmonary function, with girls showing a stronger effect than boys. In addition, among adolescent athletes we found a high prevalence of passive smoke exposure, especially among boys, and a substantial exposure to peers who smoke. Our group of overall healthy, athletic teenagers, a group we would least expect to show manifestations from passive smoking, showed clear evidence of its effects.

As stated in the 1986 American Academy of Pediatrics statement on the hazards of involuntary smoking in children,[28] there is an urgent need for immediate action to reduce passive smoking in children. Pediatricians should be aware of the extent of exposure in their patients, the harmful effects, and the need to consider passive smoking in the differential diagnosis of chronic cough and decreased pulmonary function in adolescents.

ACKNOWLEDGMENT

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ANOREXIA NERVOSA—SIGNS TO WATCH FOR

Dr. Paul Garfinkel, a psychiatrist with Toronto General Hospital, estimates that severe anorexia nervosa is prevalent in about 1 percent of the female population and mild to moderate anorexia nervosa in about 2 to 3 percent of Americans. The prevalence of bulimia, another eating disorder, is about 10 percent. Garfinkel has listed several early warning signs that should alert physicians to the possibility of anorexia nervosa. These include:

Changing weight goals—"A young woman who reaches her weight-loss goal and immediately sets a subsequent goal could be a prime candidate for anorexia nervosa," Garfinkel says.

Dieting in isolation—Most dieters want to be with other dieters; isolated dieting should be regarded warily.

Dieting and increasing criticism—Most dieters are delighted when they have lost weight. A successful dieter who remains self-critical should be watched, says Garfinkel.

Amenorrhea—The cessation of menses is an early warning sign of anorexia nervosa.

Physicians who see these signs in patients should provide "common-sense" advice and counseling. Also, says Garfinkel, physicians might "avoid doing harm" by not prescribing dieting in patients they think may be at risk for anorexia nervosa.

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SUMMARY: This study investigated the relationship of acute lower respiratory illness (LRI) to level and change in level of forced expiratory volumes in a cohort of 801 children, followed longitudinally for a maximum of 13 yr. The co-occurrence of respiratory illness before 2 yr of age and two or more LRI during a single surveillance year was associated with a 20.3% lower mean cross-sectional level of FEF25-75, and with reduced longitudinal change in level of FEF25-75. The effect of LRI on lung function was uniformly stronger for boys than for girls. Of the children with illness before 2 yr of age and two or more LRI, six of 14 were male asthmatics with mean levels of FEF25-75 that were lower than those of other asthmatic children. Pneumonia and/or hospitalization for respiratory illnes prior to the onset of study were associated with lower cross-sectional levels of forced expiratory volumes at entry to the study, even when asthmatics/persistent wheezers were eliminated from the analysis (6.1% lower level of FEV1 for a nonasthmatic boy with previous hospitalization versus a nonasthmatic boy without hospitalization). In the longitudinal analysis, pneumonia and/or hospitalization were associated with slower increase in level of forced expiratory volumes, even after adjusting for "ever diagnosis of asthma/current any wheeze" (starting at the same level, after eight years a boy with hospitalization would develop a 5.0% lower FEV1 than a boy without hospitalization). Acute LRI also was evaluated as a predictor of chronic respiratory symptoms. A strong association was found between previous hopitalization and subsequent chronic cough (Odds Ratio [OR]= 3.8)/chronic phlegm (OR= 7.1) at entry to the study; eight years later, smoking was the only significant predictor of these symptoms, and no hospitalized child had taken up smoking. Future studies may enable us to explore interactions between severe respiratory illness in early childhood and the effect of cigarette smoke or indoor/outdoor air pollution.

Acute Lower Respiratory Illness in Childhood as a Predictor of Lung Function and Chronic Respiratory Symptoms[1-3]

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Introduction

Acute lower respiratory illness (LRI) in early childhood has been proposed as a risk factor, independent of the effect of cigarette smoke, for lower level and slower growth of lung function in later childhood and for faster decline of lung function in adulthood (1, 2). Because wheeze is often a manifestation of an acute LRI in childhood whether or not a child has asthma, separation of the effects of asthma and other acute respiratory illnesses (infections) on level and growth of lung function in children is complicated. Asthma or bronchial responsiveness may alter level and change in level of lung function or predispose to increased severity of LRI, and may account for the association of LRI with alterations in lung function development. Severe infection in early childhood may, on the other hand, alter the course of asthma or predispose towards bronchial responsiveness and its subsequent effects on lung function.

As part of a longitudinal, population-based study of early-life risk predictors for chronic obstructive lung disease in adult life, the relationship between lung function and several measures of acute LRI in childhood was investigated. The results suggest that in the population studied, only the more severe acute LRI, particularly those requiring hospitalization, may be associated independently with subsequent lower level and slower growth of lung function in children.

Methods

The details of the initial selection and screening of the population have been published previously (3-5). A 34% random sample was selected from all children 4 to 10 yr of age in the public and parochial schools of East Boston, Massachusetts, as of September 1974. Between January and June 1975, interviewers visited the households of the index children who had been selected. They enumerated all residents of the households, and these residents, plus the index children, constituted the initial study population. All available members of the cohort have been screened

on an annual basis since 1975, except for the second and third screenings, which were limited to the index children as part of a special study to assess prospectively their acute respiratory illness experience.

Standardized questionnaires were used to obtain baseline histories of respiratory symptoms and illnesses, as well as smoking histories and demographic data. Parents answered the questionnaire for children 10 yr of age and younger, except those questions that pertained to the child's smoking history; all others answered for themselves.

The acute respiratory illness experience for the index children in the 5- to 11-yr-old category as of September 1975 was then assessed prospectively over a 2-yr period (6). Parents of the children were contacted by telephone every 2 wk (except in July and August) from September 1975 through June 1977; a brief questionnaire about illness symptoms was administered. Children who experienced one or more selected respiratory symptoms for two days or more in the previous 2 wk were visited in their homes, and a more detailed history of their respiratory symptoms was obtained by an interviewer-administered questionnaire. Acute lower respiratory illness was defined as acute symptoms of phlegm from the chest or pleuritic chest pain with or without wheeze that lasted 48 h or more. Wheeze alone was

not considered an adequate criterion for an acute LRI.

Subjects performed forced vital capacity (FVC) maneuvers annually with the use of an 8-L water-filled, portable recording spirometer (Survey Spirometer; Warren Collins, Braintree, MA) while in the sitting position and without the use of a noseclip. The maximum value for each measure of lung func-

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tion was obtained from values derived from five acceptable tracings. Standard criteria for curve acceptability and flow measurements were used. All lung function measurements were corrected to BTPS and were converted into percent predicted values with the nomograms of Dickman and coworkers (7).

Data Analysis

Six measures of acute lower respiratory illness were considered as predictors of level and change in level of the maximum FEV_1, FVC, and FEF_{25-75}: (1) Acute LRI at Study Year 2, (2) Acute respiratory illness before 2 yr of age, defined as a parent's reporting that the child had had croup, bronchiolitis, bronchitis, or pneumonia, (3) Acute respiratory illness before age 2 yr combined with acute LRI at Study Year 2, (4) Pneumonia prior to entry into the study, as reported by the parent, (5) Hospitalization for respiratory illness prior to entry into the study, as reported by the parent, and (6) Pneumonia and hospitalization for respiratory illness prior to entry into the study.

For each of the measures of LRI experience, mean percent predicted lung function levels were plotted by examination year as an initial exploration of possible differences in level of lung function between groups with and without respiratory illness exposure. Standard methods of multiple linear regression were then applied to assess measures of prestudy LRI experience (illness before 2 yr of age, pneumonia, or hospitalization), as predictors of level of lung function at entry to the study. Acute LRI experience reported during Study Year 2 was considered as a predictor of level of lung function in the subsequent year. Cross-sectional multiple linear analyses were adjusted for maternal smoking, but not for personal smoking, because there were no subjects with adequate data for the analyses who smoked in the years under consideration (Study Years 1 to 3). Pulmonary function and height were expressed in natural logarithms in cross-sectional analyses to stabilize the variance of the residuals. Because in the cross-sectional analyses lung function was expressed in natural logarithms, the partial regression coefficients or "parameter estimates" express the adjusted logarithmic difference in lung function between those exposed and those not exposed to a particular covariate. Thus, the "parameter estimates" express the adjusted ratio of lung function of those exposed to those unexposed to a particular covariate.

The association between each of the six measures of acute lower respiratory illness experience and change in level of lung function, measured over a maximum of 13 yr, was assessed with a Markov-type autoregressive model. Details of the autoregressive model and its application to assessment of change in lung function of children have been previously published (5, 8). Level of lung function (FEV_1, FEF_{25-75}, or FVC) at any given survey was considered as a function of mean level of lung function at the previous survey, age

in years at the current survey, sex, height, change in height over 1-yr intervals, an interaction between height and age; and an interaction between sex and age. For the purposes of presentation of results of longitudinal models, these factors are called "growth factors." Level of lung function also was considered as a function of personal smoking status and mother's smoking status at the previous survey. For each child, only pairs of data spaced one year apart were used. While this approach to longitudinal data analysis is considered relatively efficient, it does result in nonutilization of non-equidistant data points. Continuous variables, other than the dependent variable, were centered around their median values. As in the cross-sectional analyses, pulmonary function and height were expressed as natural logarithms. The "parameter estimates" in the longitudinal models, when exponentiated, made it possible to project the adjusted ratio of lung function of an exposed subject to the lung function of a subject unexposed to a particular covariate, after a given period of time, assuming that the subjects started at the same level of function (5, 7) (see table 3 for a specific example).

Examination of the distribution of residuals (observed-predicted values) was used to assess the goodness of fit of the model in relation to height, age, and previous level of lung function. The stability of the parameter estimate of interest was assessed by an examination of the distribution of parameter estimates obtained by multiple fittings of the model. Each time the model was fit, all the data points from one subject were eliminated.

Separate analyses were performed to assess whether any of the six measures of acute lower respiratory illness experience had an effect on change in level of lung function independent of the effect of these other variables that had been previously established to effect change in level of lung function (5, 9, 10). Analyses were performed with and without children with doctor's diagnosis of asthma or mother's report of child's persistent wheeze at entry to the study; also with and without adjustment for "ever diagnosis of asthma," if there was a current report of any wheeze. To examine whether there were sex-specific effects of acute LRI on lung function, sex-stratified models also were examined.

Although analyses that assessed change in level of lung function are based on a maximum of 13 yr of data, the percent of the 801 children lost to follow-up increased considerably after Study Year 8 (up to Year 8 loss to follow-up averaged less than 3% per yr; for Years 8 to 12, loss to follow-up averaged 13% per yr). The number of boys with a history of hospitalization who continued to participate in the study was stable from Years 1 through 9. Over the subsequent four-year period, there was a 64% drop in participation of this subgroup from 25 to 9 boys. The autoregressive model, therefore, cannot be used with confidence to project beyond eight years what the differences in longitudinal change

in level of lung function would be for two hypothetical children with and without early childhood acute LRI exposures.

Acute lower respiratory illness experience as a predictor of subsequent respiratory illness and symptoms also was evaluated. Hospitalization for respiratory illness prior to entry to the study was examined as a predictor of respiratory symptoms at entry to the study (t), at t + 5 yr, and at t + 8 yr. These time intervals were selected because beyond eight years sufficient data on symptoms were unavailable for the reason specified above.

For this analysis, persistent wheeze was defined as wheeze occurring most days or nights. Chronic cough was defined as cough on most days for as much as three months of the year; chronic phlegm as phlegm, sputum, or mucus from the chest on most days for as many as three months of the year. "Debilitating chest illness" was defined as chest illness that kept a child from his/her usual activities for as much as three days in a week.

Results

Characteristics of the Cohort

There were 421 index children and 380 siblings for a total of 801 children available for analysis. Analyses that assessed LRI in Study Year 2 as a predictor used only the subset of index children with acceptable data; all other analyses included the siblings. No systematic differences were seen between the children included versus those excluded from the various analyses because of missing data on one or another of the variables. Of the 801 index children and their siblings, 22.3% had had illness before age 2 yr, 13.5% had had pneumonia, and 8.6% had been hospitalized for respiratory illness prior to study onset. Of the index children studied during Year 2, 14.2% had two or more LRI during that year.

The indicators of LRI were correlated with each other and with a history of asthma and persistent wheeze. LRI at Study Year 2 was associated with illness before age 2 yr (OR = 2.0; 95% Confidence Interval [CI] = 1.0–4.3) and pneumonia (OR = 2.1; 95% CI = 0.9–4.8). Of the 421 index children, 7 of 29 (24.1%) children with a history of hospitalization for acute respiratory illness prior to entry to the study had ≥ 2 LRI, whereas 43 of 320 (13.4%) of those not hospitalized had ≥ 2 LRI.

Those children with a history of hospitalization prior to entry into the study (n = 69) were more likely to have had pneumonia (OR = 12.5; 95% CI = 7.0–22.3) and illness before age 2 yr (OR = 7.7; 95% CI = 4.2–14.3) that children who had not been hospitalized. They were also

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more likely to have entered the study with a doctor's diagnosis of asthma (OR = 9.9; 95% CI = 5.0-19.3). At entry into the study, 55% of the children with a history of hospitalization had pneumonia; 75.4% had illness before age 2 yr, and 30.4% had a doctor's diagnosis of asthma. In contrast, the prevalence of asthma in the nonhospitalized population was 4.2%. Eight years after entry to the study, of the children previously hospitalized, 35.5% had ever had a diagnosis of asthma, as compared to 10.7% of the children not hospitalized prior to entry to the study (OR = 4.6; 95% CI = 1.9-10.9).

Acute LRI as a Predictor of Lung Function

Cross-sectional level of FEV_1 at Study Year 3 was not lower for children with ⩾ 2 LRI during Study Year 2, after adjustment for the effects of age, height, sex, and maternal smoking (parameter estimate for LRI = -0.0211, p = 0.38). Among the children without asthma or persistent wheeze, there was also no association between level of FEF_{25-75} and ⩾ 2 LRI, although an association was suggested when the asthmatic children were included in the analysis (parameter estimate for LRI = -0.0903, p = 0.054).

An association was noted between lower cross-sectional level of FEF_{25-75} and having had *both* illness before age 2 yr and ⩾ 2 LRI at Study Year 2. Of the 14 children with this repeated LRI experience, only three had an FEF_{25-75} greater than 75% predicted at entry to the study. Only two of the children were girls; 12 (85%) were boys, six of whom had either a doctor's diagnosis of asthma or

persistent wheeze on initial examination (table 1). For the boys, mean cross-sectional percent predicted levels of FEF_{25-75} were low both at entry to the study and for each of the subsequent 12 examination periods (figure 1). The subgroup of six boys with asthma or persistent wheeze who had both illness before age 2 yr and ⩾ 2 LRI also maintained mean levels of percent predicted FEF_{25-75} that were persistently lower than all other boys who at entry had asthma/persistent wheeze without the same history of LRI (n = 17 at Study Year 3; yearly data for mean FEF_{25-75} by subgroup not shown).

Adjusting for age, height, sex, and maternal smoking, the mean cross-sectional level of FEF_{25-75} at Study Year 3 was 20.3% lower (p = 0.003) for the children with both illness before 2 yr of age and ⩾ 2 LRI (n = 11 for those with sufficient data on all variables), than for all other children, and remained lower after adjusting additionally for asthma/persistent wheeze. Although differences were not significant, children with both illness before 2 yr of age and ⩾ 2 LRI also tended to have a higher FVC than other children. At Study Year 3, children with illness before age 2 yr but without ⩾ 2 LRI at Study Year 2 (n = 28) had adjusted cross-sectional levels of FEF_{25-75} similar to the levels of the children with no lower respiratory illness experience (n = 172) and the levels of the children with only ⩾ 2 LRI but no illness before 2 yr of age (n = 20). In the longitudinal analysis, no association was found between ⩾ 2 LRI at Study Year 2 and slower increase in level of FEV_1 or FEF_{25-75} (parameter estimate of LRI = 0.0034, p = 0.48; and -0.0044, p = 0.63 for FEV_1 and

FEF_{25-75}, respectively), after adjustment for previous level of lung function, sex, age, height, their interactions, and smoking. These conclusions did not change if the longitudinal analyses were restricted to observations for children younger than 12 yr of age.

The increase in level of FEF_{25-75} was slower (parameter estimate = -0.0509, p = 0.006) for the children with both illness before 2 yr of age and ⩾ 2 LRI at Study Year 2, compared to the rest of the population; this association remained significant even after additional adjustment for "ever diagnosis of asthma and current any wheeze" and after restriction of the analysis to the boys alone. The increase in level of FVC, on the other hand, was significantly faster for the children with both illness before 2 yr of age and ⩾ 2 LRI (parameter estimate = 0.0262, p = 0.011); this association also remained significant after additional adjustment for "ever diagnosis of asthma and current any wheeze."

Illness before 2 yr of age, pneumonia prior to entry into the study, and hospitalization prior to entry into the study were evaluated as predictors of cross-sectional level and longitudinal increase in level of lung function for the entire cohort of 801 children. Mean cross-sectional levels of percent predicted FEF_{25-75} for boys (not girls) with illness before 2 yr of age tended to be lower throughout the 13 years of the study (figure 2). Mean levels of percent predicted FEV_1 for those boys (not girls) with illness before 2 yr of age were lower only in the first two examination years. Significant associations were found between illness before 2 yr of age and lower cross-sectional adjusted levels of FEV_1 and FEF_{25-75} on entry to the study only when children with asthma/persistent wheeze were included in the cross-sectional analyses (parameter estimate for FEF_{25-75}, including children with asthma/persistent wheeze = -0.06791, p = 0.05; parameter estimate excluding them = -0.0468, p = 0.16). Stratification by sex did not strengthen the associations of interest for the nonasthmatic children. Illness before 2 yr of age was not a significant predictor of longitudinal increase in level of FEV_1, FVC, or FEF_{25-75}, after adjustment for growth factors and smoking.

Of the children with asthma/persistent wheeze, a similar influence was found in relation to the cross-sectional association between pneumonia and a lower lung function level at entry to the study. Pneumonia was significant as a predictor of

TABLE 1

RELATIONSHIP BETWEEN ILLNESS BEFORE 2 YR OF AGE AND LOWER RESPIRATORY ILLNESS AT STUDY YEAR 2, STRATIFIED BY ASTHMA OR PERSISTENT WHEEZE AND BY SEX

	No Illness before 2 yr of Age (n)		Illness before 2 yr of Age (n)	
	0-1 LRI	⩾ 2 LRI	0-1 LRI	⩾ 2 LRI
Diagnosis of Asthma or Persistent Wheeze				
No				
Female	102	17	17	2
Male	124	14	22	6
Yes				
Female	9	1	4	0
Male	15	3	5	6
Total	250	35	48	14

Definition of abbreviation: LRI = lower respiratory illness.

FEV(1)   BOYS   FEF(25-75)

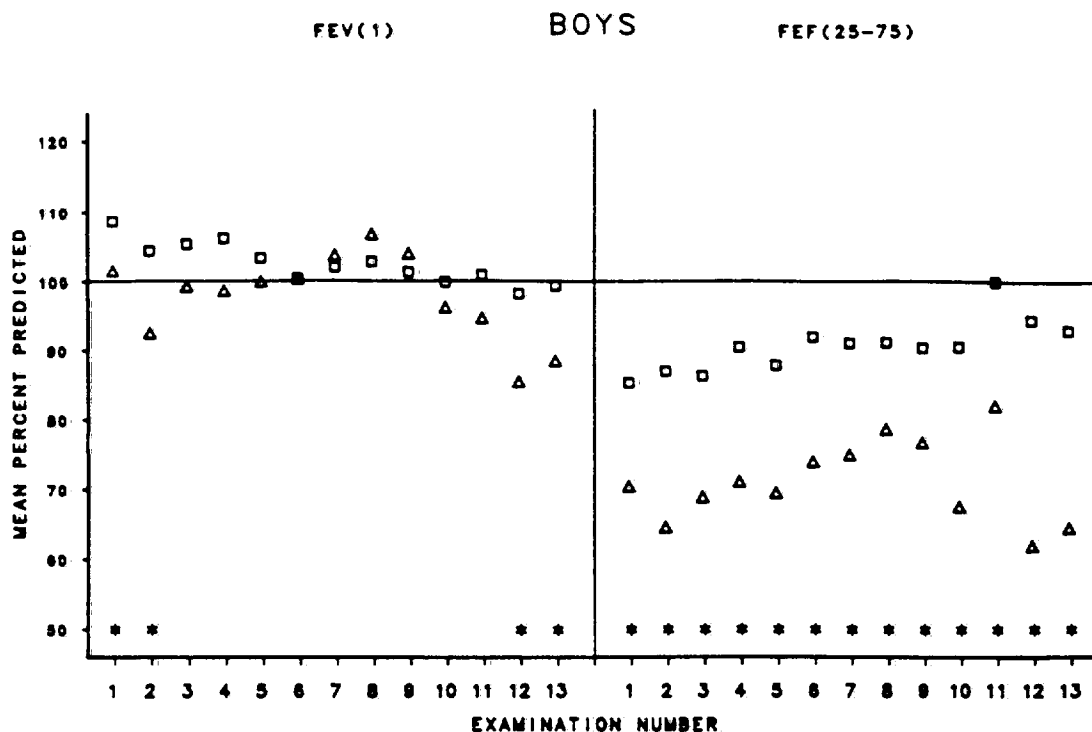

Fig. 1. Mean percent predicted FEV, and FEF$_{25-75}$ at each annual examination (1 to 13) in index boys (n = 244) classified according to acute respiratory illness experience. Triangles = boys with both illness before 2 yr of age and also > 2 lower respiratory illnesses at Study Year 2. Squares = all other boys (those without both illness before 2 yr of age and also > 2 lower respiratory illnesses at Study Year 2). The asterisks represent pairs of values ± 1 SE that do not overlap.

FEV(1)   BOYS   FEF(25-75)
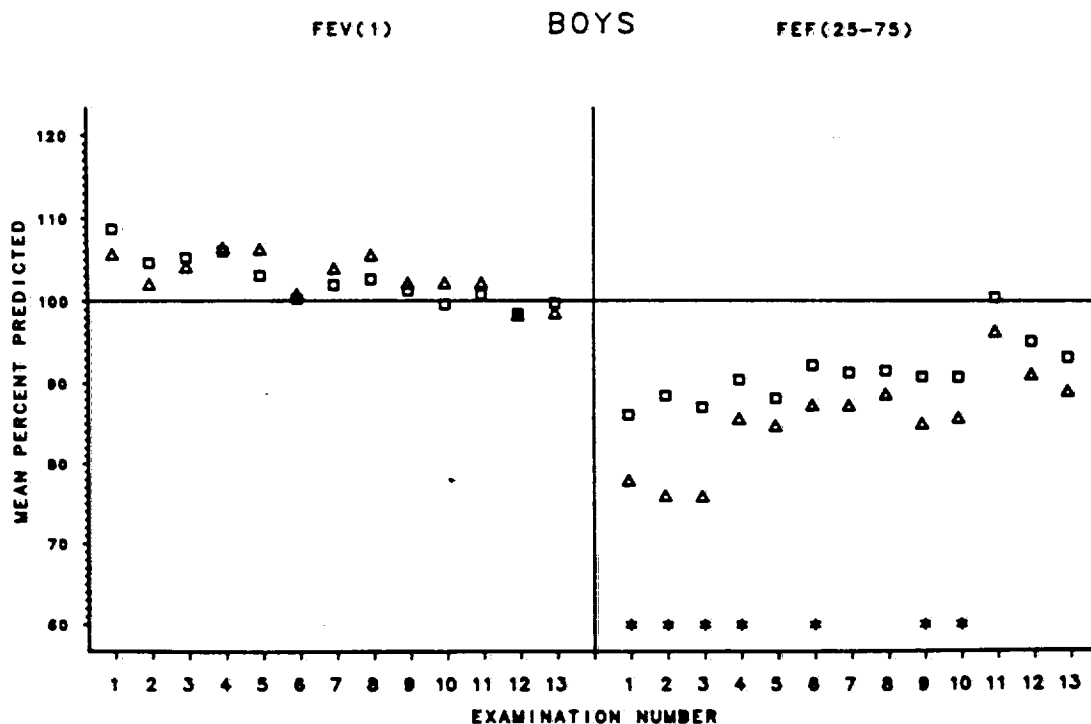
Fig. 2. Mean percent predicted FEV, and FEF$_{25-75}$ at each annual examination (1 to 13) in boys (n = 422 and includes index boys and male siblings) classified according to presence or absence of history of illness before 2 yr of age (bronchitis, bronchiolitis, croup, or pneumonia). Triangles = boys with illness before 2 yr of age; squares = boys without illness before 2 yr of age. The asterisks represent pairs of values ± 1 SE that do not overlap.

entry level of FEV_1 (parameter estimate = -0.0439, p = 0.02) in a regression model that included all children and adjusted for age, sex, height, and maternal smoking. In a sex-stratified model, a history of pneumonia was a significant predictor of lower level of FEV, for boys (parameter estimate = -0.0614, p = 0.018), but not for girls (parameter estimate = -0.0248, p = 0.38). When children with asthma/persistent wheeze were excluded from the models, there was a reduction in the strength of the association between pneumonia and lower initial level of FEV_1 for the entire cohort (parameter estimate = -0.0350, p = 0.10), and for boys alone (parameter estimate = -0.0440, p = 0.12).

In the longitudinal analysis, there was a significant association between a history of pneumonia and a slower rate of increase in level of FEF_{25-75} for boys, but not for girls. This association for boys remained after additional adjustment for "ever diagnosis of asthma/current any wheeze" (parameter estimate for pneumonia = -0.0252, p = 0.02).

Hospitalization for respiratory illness prior to entry to the study was the strongest predictor of cross-sectional level of lung function, independent of the influence of a history of asthma or persistent wheeze. Sex stratification demonstrated that a consistent pattern of lower mean percent predicted FEF_{25-75} was present for boys with a history of hospitalization (figure 3), but not for girls (figure not shown). In the first nine years of the study, boys with a history of hospitalization, but not girls, tended to have a lower mean percent predicted FEV_1.

At entry to the study, a history of hospitalization was associated with a level of FEV_1 that was lower than for children without a history of hospitalization (parameter estimate = -0.0654, p = 0.004) (table 2) and remained significant after removing the children with asthma or persistent wheeze from the analysis (parameter estimate = -0.0626, p = 0.025). Level of FEF_{25-75} (table 2) and FVC. adjusted for age, height, and sex, also tended to be lower among the hospitalized children, although not significantly so, particularly after exclusion of the children with asthma/persistent wheeze.
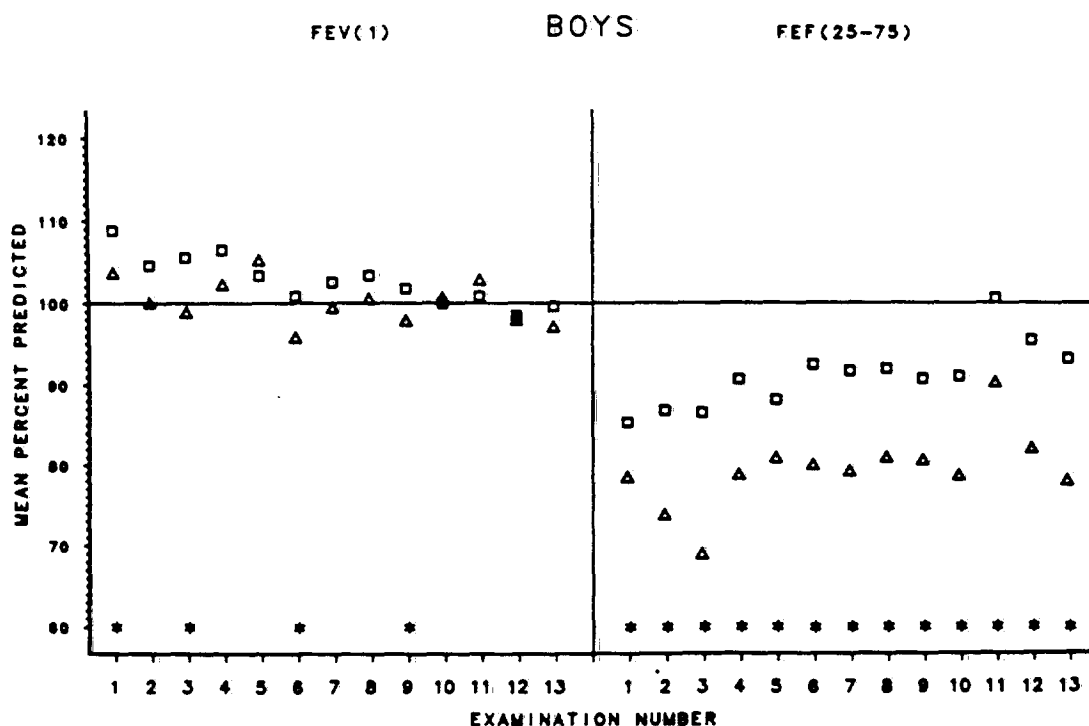
TABLE 2

REGRESSION EQUATIONS RELATING LEVEL OF LUNG FUNCTION TO HOSPITALIZATION FOR RESPIRATORY ILLNESS BEFORE ENTRY TO STUDY, AFTER ADJUSTMENT FOR AGE, HEIGHT, SEX, AND MATERNAL SMOKING

Dependent Variables	In FEV_1 (L) R-square = 0.60			In FEF_{25-75} (L/s) R-square = 0.14		
	Regression Coefficient	Standard Error	p Value	Regression Coefficient	Standard Error	p Value
Intercept	-6.1345	0.4062	0.0001	-4.5511	0.9386	0.0001
Age at entry, yr	0.0364	0.0064	0.0001	0.0208	0.0147	0.1581
Lung height at entry, inches	1.6234	0.1117	0.0001	1.3022	0.2581	0.0001
Sex at entry (1 = male)	-0.0622	0.0128	0.0001	-0.0054	0.0295	0.8545
Maternal smoking (1 = current)	-0.0149	0.0130	0.2548	-0.0768	0.0302	0.0114
Hospitalization (1 = yes)	-0.0654	0.0226	0.0040	-0.0962	0.0522	0.0662

FEV(1)   BOYS   FEF(25-75)

Fig. 3. Mean percent predicted FEV_1 and FEF_{25-75} at each annual examination (1 to 13) in boys (n = 422) classified according to presence or absence of history of hospitalization for respiratory illness prior to entry to study. Triangles = boys with history of hospitalization; squares = boys without history of hospitalization. The asterisks represent pairs of values ± 1 SE that do not overlap.

TABLE 3

PARTIAL REGRESSION COEFFICIENTS REFLECTING RELATIONSHIPS BETWEEN CHANGES IN LEVEL OF LUNG FUNCTION OVER TIME AND OTHER COVARIATES*†

Dependent Variables	In FEV_1 (L)			In FEF_{25-75} (L/s)		
	Regression Coefficient	Standard Error	p Value	Regression Coefficient	Standard Error	p Value
Previous level of In lung function	0.7341	0.0104	0.0001	0.7188	0.0107	0.0001
Maternal smoking (1 = current)	-0.0065	0.0028	0.0187	-0.0223	0.0054	0.0001
Personal smoking (1 = current)	-0.0102	0.0007	0.1207	-0.0230	0.0127	0.0712
Hospitalization (1 = yes)	-0.0104	0.0053	0.0503	-0.0359	0.0104	0.0006

* After adjustment for previous level of lung function, age, sex, height, age*change in height, and sex*height.

† Using the equation from Rosner and colleagues (8):

$$E(y_{i,t_{i}} + r y_{i,t_{i}} + t) = \beta\Delta(1 - \gamma)(1 - \gamma).$$

the estimate of the ratio of the FEV_1 of the hospitalized child to the FEV_1 of the nonhospitalized child after one yr is exp (-0.0104) = 99.0%. The FEF_{25-75} of the hospitalized child to the FEF_{25-75} of the nonhospitalized child after one yr is exp (-0.0359) = 96.5%. These short-term projections assume that the children start at the same level of lung function and show the same growth in height over the 1-yr period.

In sex-stratified models, the associations between hospitalization and lower cross-sectional level of lung function, as described in the previous paragraph, were seen for boys but not for girls. Of the 69 children with a history of hospitalization at entry to the study, 60.9% were boys; there was a more equal proportion of boys and girls among those not hospitalized (table 4).

In the longitudinal analysis, after adjustment for "growth factors" and smoking, hospitalization was a significant predictor of change in level both of FEV_1 (parameter estimate = -0.0104, p = 0.05) and FEF_{25-75} (parameter estimate = -0.0359, p = 0.0006) (table 3), but not change in level of FVC. After additional adjustment for "ever diagnosis of asthma and current any wheeze," the association between a history of hospitalization and slower increase in forced expiratory volume remained significant. In a sex-stratified model, the association between hospitalization and slower increase in level of both FEV_1 (parameter estimate = -0.0134, p = 0.05) and FEF_{25-75} (parameter estimate = -0.0373, p = 0.004) remained significant for boys but not for girls, even after adjustment for "ever diagnosis of asthma and current any wheeze."

The smaller subgroup of children with both a history of hospitalization and a history of pneumonia prior to entry to the study (n = 17) was compared to the rest of the population. In the longitudinal analysis, the children had slower increase in level of FEF_{25-75} than the rest of the population after adjustment for "growth factors," smoking, and "ever asthma and current any wheeze" (param-

eter estimate for hospitalization and pneumonia = -0.0308, p = 0.03). In contrast to results for the larger group of children with a history of hospitalization, this negative association remained significant even after eliminating those with asthma/persistent wheeze at entry to the study.

Acute Lower Respiratory Illness as a Predictor of Subsequent Respiratory Symptoms

At entry to the study, when compared with children with no history of hospitalization for respiratory illness, children with a history of hospitalization had a higher prevalence of "any wheeze" (OR = 4.3; 95% CI = 2.4-7.5), persistent wheeze (OR = 5.3; 95% CI = 2.8-10.0), chronic cough (OR = 3.8; 95% CI = 2.0-7.2), and chronic phlegm (OR = 7.1; 95% CI = 2.8-18.2) (table 4). Over an eight-year period of follow-up, although the subjects with a history of previous hospitalization maintained a higher prevalence of "any wheeze," they had a steep reduction in the prevalence of symptoms of persistent wheeze, chronic cough, and chronic phlegm (table 4). The nonhospitalized group, on the other hand, developed an increasing prevalence of chronic cough and phlegm, predominantly among the smokers. Of those nonhospitalized children, smokers had 2.9 times as much chronic cough (95% CI = 1-8.2) and 10.9 times as much chronic phlegm (95% CI = 2.4-39.4) as the nonsmokers

TABLE 4

COMPARISON OF CHILDREN WITH AND WITHOUT HISTORY OF HOSPITALIZATION FOR RESPIRATORY ILLNESS PRIOR TO ENTRY TO THE STUDY

Hospitalized	Entry Year (t)		t + 5		t + 8	
	Yes	No	Yes	No	Yes	No
Number	69	731	40	546	31	460
Age (mean)	6.7	6.9	11.7	11.8	14.5	14.7
Sex						
Male, %	60.9	52.0	75.0	51.5	74.2	50.0
Female, %	39.1	48.0	25.0	48.5	25.8	49.5
Doctor's diagnosis of asthma at entry, %	30.4	4.2	32.5	4.4	29.0	5.2
Ever asthma, %	30.4	4.2	37.5	8.2	35.5	10.7
Persistent wheeze, %	27.5	6.7	2.5	0.7	0.0	0.9
Any wheeze, %	60.6	30.5	35.0	9.5	29.0	14.8
Chronic cough, %	24.6	7.9	0.0	1.5	0.0	4.4
Chronic phlegm, %	13.0	2.1	0.0	0.002	0.0	2.0
Bouts of cough/phlegm > 1 wk, %	56.5	28.0	1.0	5.2	9.7	11.5
Debilitating chest illness in past yr, %	60.9	26.8	1.0	2.7	6.5	4.1
Pneumonia before entry, %	55.1	9.4	47.5	10.0	54.8	10.0
Illness before age 2 yr, %	75.4	28.3	70.0	31.0	77.4	30.5
Maternal smoking, %	56.5	55.0	65.0	55.3	54.8	51.9
Personal smoking, %	0.0	0.0	0.0	3.1	0.0	16.5
FEV_1						
Mean % predicted	110.3	114.8	100.7	107.0	102.0	106.4
for nonwheezers, nonsmokers*					104.3 (n = 20)	107.0 (n = 282)
for smokers*						105.4 (n = 56)
FEF_{25-75}						
Mean % predicted	83.8	91.1	86.2	95.1	86.4	98.1
for nonwheezers, nonsmokers*					90.2 (n = 20)	100.5 (n = 282)
for smokers*						92.0 (n = 56)

* The number of children in these categories is smaller than the total number of children for whom symptom data is available because there were fewer children who successfully performed the forced expiratory maneuvers.

(table 4). The previously hospitalized and nonhospitalized nonsmokers had a similarly low prevalence of chronic respiratory symptoms. Of note, 16.6% of the nonhospitalized children who were surveyed eight years after entry to the study had taken up smoking, whereas none of the hospitalized children had done so.

Discussion

For nonasthmatic children, report of pneumonia or hospitalization prior to this study were the strongest predictors of subsequent reduced level and growth of lung function. Many of the children with a history of LRI both in infancy and at school age had asthma or persistent wheeze by the time they entered the study. Children with $\geq$ 2 LRI in Study Year 2 did not have preexisting or subsequent lower level of lung function unless they also had a history of LRI before 2 yr of age. These data are consistent with the hypothesis that events in the prenatal period and in infancy may be more important determinants of lung function in later childhood than events in the school-age period.

To understand the detailed implications of the study, several of its limitations need to be addressed. Martinez and colleagues (11) have suggested that some infants have preexisting diminished pulmonary function that puts them at greater risk for acute wheezing LRI. In their study, preexisting diminished lung function was not a risk factor for LRI without wheeze. Our study design does not allow us to determine whether low lung function preceded LRI in infancy, or whether LRI in infancy preceded low lung function. Nor does it allow us to determine the role of wheeze in predicting the relationship between LRI and lung function in infancy. Our study was designed to examine the effect of LRI in the school-age years on subsequent lung function in asthmatic and nonasthmatic children. Although it has detailed prospective data on 5- to 11-yr-olds, it suffers from the potential for recall bias relating to early childhood illnesses. In this study we were unable to validate the reporting of hospitalization. It is unlikely, however, that parents would selectively recall previous hospitalization in sicker children because, regardless of subsequent events, early childhood hospitalization is usually experienced as a major event in family life.

As described above, loss to follow-up limits the age range within which this study can confidently make longitudinal projections. In addition, the estimates of the precision of these projections are limited because statistical techniques have not yet been developed for establishing confidence intervals around mean change in level of forced expiratory volumes for exposed and unexposed subjects. Because severe acute respiratory illness is a relatively rare event, this study also lacks the power to evaluate some aspects of the relationship between illness and level of lung function, particulary after stratifying by sex and controlling for asthma and smoking. Numbers of events are too small to explore potential interactions between passive smoking and previous hospitalization in their relationship to subsequent lung function. Since none of the previously hospitalized children with adequate smoking data took up smoking, this study cannot predict the extent to which these children would have been, as active smokers, at increased risk for lung function deficits. The lack of smoking in children previously hospitalized for respiratory illness may represent a "healthy smoker effect," where individuals who are constitutionally less comfortable smoking chose not to take up the habit.

Our study supports the observations of others that males appear to be more at risk for respiratory illness in infancy than females. The Tecumseh and Chapel Hill studies have noted the excess of LRI among male infants, but not among 5- to 11-yr-old boys as compared to girls (12-14). Taussig (15) has suggested that the early LRI in male subjects may reflect the preponderance of males with smaller airways for lung size (referred to as dysynapsis by Green and Mead [16, 17]), and that the equalizing of sex-specific LRI rates in school-age children may coincide with the growth spurt during which males acquire an airway size/lung size ratio similar to that present in females.

Martin and colleagues (18) suggest that in the adolescent years male asthmatics appear to improve more than female asthmatics. In our study, male subjects with illness before 2 yr of age and $\geq$ 2 LRI at Study Year 2, half of whom were asthmatic, did not appear to catch up to their peers (asthmatics or nonasthmatics) in the adolescent years. They had a slower increase in level of FEF_{25-75} than the rest of the cohort, and a faster increase in level of FVC, which at entry to the study was equal to or higher than the mean FVC in the rest of the cohort. This would support an association between dysynapsis, male sex, an early history of asthma, and frequent LRI in childhood as well as in infancy.

Cross-sectional modeling suggests that for nonasthmatic subjects, previous hospitalization for acute respiratory illness is independent of the effect of passive smoking, associated with a deficit in FEV_1 at entry to the study. The model predicts that a nonasthmatic 7-yr-old boy with no passive smoking experience, but with previous hospitalization for respiratory illness, would have a 6.1% lower level of FEV_1 than a nonasthmatic boy with neither hospitalization nor passive smoking experience. The model (table 2) also predicts that passive smoking together with hospitalization would be associated with a 7.5% deficit.

The sex-stratified longitudinal model that includes all boys suggests that if two hypothetical 6-yr-old boys, one with a history of hospitalization and one without such a history, started at the median height and FEV_1 for their age, then eight years later the boy with a history of hospitalization would have an FEV_1 that was 5.0% lower, and an FEF_{25-75} that was 11.7% lower than that of the boy without a history of hospitalization, assuming all other factors affecting growth were equal and the boys were neither exposed to smoking nor had wheeze symptoms in the years subsequent to entry to the study. The projection also assumes that the parameter estimate is applicable over the 8-yr period.

Nonwheezing boys with no smoking exposure, but with *both* previous hospitalization and pneumonia, would, after eight years, have an FEF_{25-75} that was 11.8% lower than other nonwheezing boys without hospitalization and pneumonia, projecting from a model that excludes those with history of asthma or symptoms of persistent wheeze at entry to the study. The East Boston study follows children at least into the mid-teens, but since lung growth may continue into the late teens and early twenties, more follow-up time is needed to determine whether or not those children identified as persisting at lower levels of function as teenagers remain impaired as adults, and is the group of nonsmokers at greatest risk of developing chronic obstructive lung disease.

Although this study found associations between early childhood acute respiratory illness and subsequent development of chronic respiratory symptoms and cough at entry to the study, there

were no effects that were maintained over a period of eight years in nonsmokers. Personal smoking was the overwhelming predictor of subsequent cough and phlegm, and none of the children who reported previous hospitalization prior to study onset took up smoking. These results differ from the results of the large prospective study of children in the United Kingdom reported by Kiernan, Colley and colleagues (19), which found long-term effects of childhood respiratory illness on the long-term development of chronic cough. An interaction between higher air pollution levels in the United Kingdom and the effect of early childhood illness may account for the difference in the relationship between early illness and subsequent symptoms in the cohort in East Boston as compared to the cohort in the United Kingdom (20, 21). Studies of respiratory morbidity and mortality in other populations of children may enable us to explore the interaction between severe respiratory illness in early childhood and the effect of other exposures such as cigarette smoke and indoor or outdoor air pollution.

Acknowledgment

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SUMMARY: Results   are   presented   from   a   second
cross-sectional assessment of the association of air pollution with
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Cities Study of Air Pollution and Health.   Air pollution
measurements collected at quality-controlled monitoring stations
included total suspended particulates (TSP), particulate matter
less than 15 um (PM_{15}) and 2.5 um (PM_{2-5}) aerodynamic diameter,
fine fraction aerosol sulphate (FSO_4), SO_2, O_3, and NO_2. Reported
rates of chronic cough, bronchitis, and chest illness during the
1980-1981 school year were positively associated with all measures
of particulate pollution (TSP, PM_{15}, PM_{2-5}, and FSO_4) and positively
but less strongly associated with concentrations of two of the
gases (SO_2 and NO_2).   Frequency of earache also tended to be
associated with particulate concentrations, but no associations
were found with asthma, persistent wheeze, hay fever, or
nonrespiratory illness.   No associations were found between
pollutant concentrations and any of the pulmonary function measures
considered (FVC, FEV_1, FEV_{0-75}, and MMEF). Children with a history
of wheeze or asthma had a much higher prevalence of respiratory
symptoms, and there was some evidence that the association between
air pollutant concentrations and symptom rates was stronger among
children with these markers for hyperreactive airways. These data
provide further evidence that rates of respiratory illnesses and
symptoms are elevated among children living in cities with high
particulate pollution.   They also suggest that children with
hyperreactive airways may be particularly susceptible to other
respiratory symptoms when exposed to these pollutants.   The lack
of association between pollutant concentrations and measures of
both pulmonary flow and volume suggests, however, that these
increased rates of illness are not associated with permanent loss
of pulmonary function, at least in the preadolescent years.

Effects of Inhalable Particles on Respiratory Health of Children[1-4]

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JOHN D. SPENGLER, and BENJAMIN G. FERRIS, JR.

Introduction

A recent report (1) from the Six Cities Study of Air Pollution and Health described a strong association between frequencies of chronic cough, bronchitis, and chest illness in preadolescent school-children and concentrations of particulate and sulfur oxide air pollution in six communities in the eastern United States. Illness and symptom rates were higher by approximately a factor of two in the community with the highest air pollution concentrations compared with the community with the lowest concentrations. No association was found, however, between air pollution concentrations and two measures of pulmonary function, FVC and FEV_1. Because the health data were gathered between 1974 and 1980, only three pollutant variables, total suspended particulates (TSP), the sulfate fraction of TSP (TSO_4), and sulfur dioxide concentrations (SO_2), were consistently available for this analysis. These measurements were gathered from stations operated by a variety of public and private agencies. Analysis of limited data on spatial and temporal variability of air pollution concentrations and respiratory health within the six cities found an association between total sulfate (TSO_4) concentrations and respiratory illness and symptom rates, but not with TSP or SO_2.

These results raised several issues requiring further investigation. (1) To what extent could these results be replicated using air pollution measurements gathered under standardized procedures established as part of the Six Cities Study? (2) Was the respiratory health status of study children associated with either of two measures of size-fractionated particulate matter, aerodynamic diameter less than 15 µm (PM_{15}) and less than 2.5 µm ($PM_{2.5}$)? Did ozone (O_3) or nitrogen dioxide (NO_2) concentrations have a direct effect on respiratory health or modify the associations with other pollutants? (3) Could associations be found between air pollution concentrations and potentially more sensitive measures of small airways impairment ($FEV_{0.75}$ and MMEF) obtained from digitized analysis of the spirometric tracings? (4) Could sensitive subgroups of the study population be identified?

This study investigated each of these issues by analyzing the respiratory health of the original cohort of the school children reexamined during the 1980–1981 school year, a period during which all elements of the study's air pollution measurement program, including size-fractionated particle measurements, were available in all six cities.

Methods

Populations Studied and Survey Procedures

The cohort of school children has been described elsewhere (1–3). Briefly, the children were initially seen as first- and second-graders attending schools in study communities during the enrollment period between 1974 and 1979. Each child had had an annual follow-up examination consisting of a respiratory symptom questionnaire completed by a parent and a spirometric examination performed at school. Health data used in this report were collected during the 1980–1981 school year. Three cities were visited between September and December, 1980: Watertown, MA; St. Louis, MO; and Portage, WI. And three were visited between January and April, 1981: Kingston-Harriman, TN; Steubenville, OH; and Topeka, KS.

Five respiratory illness and symptom responses obtained from the questionnaire were considered: bronchitis, cough, chest illness,

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wheeze, and asthma (4). Bronchitis required a doctor's diagnosis in the last year; chronic cough was defined as being present for 3 months in the last year; chest illness required restriction of activities of 3 days or more. Persistent wheeze was defined as wheeze apart from colds or for most days or nights in the last year. Asthma required the reporting of a doctor's diagnosis.

Three symptoms not expected to be related to air pollution were also considered: earache, hay fever, and nonrespiratory illness or trauma that restricted activities for 3 days or more.

The spirometric examination has been described elsewhere (5). Briefly, the examination was performed using a water-filled recording spirometer (Survey Spirometer; Warren E. Collins, Braintree, MA) with the child in a sitting position without a noseclip. Each tracing was examined in the school by the local study coordinator. Those judged acceptable by standard criteria (4) were digitized centrally (6). The three best tracings varying by less than 150 ml were averaged to calculate the FEV$_1$, FEV$_{0.75}$, and FVC, and the tracing with the highest sum of FEV$_1$ and FVC was used to calculate the maximal midexpiratory flow (MMEF). All values were corrected to body temperature and pressure saturated with water (BTPS). The child's height and weight were measured in stockinged feet and recorded to the nearest centimeter and pound.

Air Pollution Measurements

A centrally located air monitoring station was established in each community at the time of the first health examination. SO$_2$, NO$_2$, O$_3$, and meteorologic variables were measured continuously. Integrated 24-h TSP samples were collected on a regular schedule. TSP samples were mailed to a central laboratory for determination of total mass concentration. Each site was audited semiannually by an independent agency using National Bureau of Standards traceable reference standards (7).

Beginning in 1978, dichotomous aerosol samplers were installed at each study site (8). The inlet of these samplers removes the larger particles (50% cut-size at 15 μm aerodynamic diameter). The aerosol is then divided into two fractions: the fine fraction with aerodynamic diameter less than 2.5 μm, and the coarse fraction between 2.5 and 15 μm. The two fractions were analyzed for mass concentration by beta-ray attenuation (9) and for elemental concentration by x-ray fluorescence (10). PM$_{15}$ is the sum of the fine and coarse fractions. All elemental sulfur has been assumed to be present as sulfate ion (SO$_4$). All dichotomous samplers were operational for at least 1 yr prior to the 1980–1981 school year.

Daily mean concentrations of SO$_2$, NO$_2$, and O$_3$ were obtained by averaging hourly concentrations for each day with at least 18 hourly values. Three measures of particle mass (PM$_{2.5}$, PM$_{15}$, and TSP) were considered, as well as the concentration of elemental sulfate in the fine fraction, denoted here as FSO$_4$.

Monthly means were calculated for each pollutant by averaging all available daily values. An air pollution exposure in the previous year was calculated for each child by averaging the monthly means for the 12 months preceding the month of the spirometric examination.

Statistical Methods

Previously reported analyses of illness and symptom rates and of pulmonary function levels established that city-to-city variation in health outcomes was larger than would be expected given interindividual variation in health outcomes (1). To account for this variability, we used two-step methods to analyze the health outcomes. In the analysis of illness and symptom rates, an initial logistic regression was used to estimate the adjusted logit of illness frequency in each of the six cities, controlling for sex, age, maternal smoking, and the presence of a gas stove in the home. In the second step, these estimated logits were regressed against the city-specific air pollution measurements using weights that were inversely proportional to the sum of the between-city variance and the within-city variance of the adjusted logits. The results of this regression are summarized here by the estimated relative odds of the illness or symptom rate in the most polluted and least polluted city. Ninety-five percent confidence intervals (95% CI) for these relative odds were calculated using Miettinen's test-based approximation (11).

For the pulmonary function measures, the same general scheme was used. In the first step, the logarithms of individual pulmonary function measurements were fitted to a linear function of the logarithm of height, age, maternal smoking, indicators for sex, parental education, gas cooking, and an interaction between sex and logarithm of height. In the second step, the adjusted city-specific means of the logarithms of pulmonary function measures were regressed on the air pollution variables. Each pollution variable was considered separately. The regression results are summarized by the estimated percentage difference in pulmonary function level between the most polluted and least polluted cities. This difference is given by the antilogarithm of the regression coefficient times the difference in pollutant concentrations. Ninety-five percent confidence intervals were calculated in the logarithmic scale, again using a test-based approximation.

A potentially sensitive subset of the population was defined by the presence of reported asthma or persistent wheeze. The two-step analysis was repeated to produce separate estimates of the air pollution associations in children with and without asthma or wheeze. In the first step, city-specific rates of respiratory symptoms were calculated for each group, after adjusting for the associations with sex, age, parental education, maternal smoking and gas stoves in the combined sample. In the second step, the city-specific adjusted rates were regressed on air pollution, separately for children with and without asthma or wheeze. An analogous procedure was used for analysis of pulmonary function measurements.

Results

A total of 8,131 children were seen during the 1980–1981 school year. Because the enrollment period varied among cities, the age distributions of these children also varied among cities. To avoid confounding caused by age and race, the analysis was restricted to the 5,422 10- to 12-yr-old white children examined in the 1980–1981 school year (table 1).

Adjustment for Covariates

Each symptom was analyzed using a logistic regression model including sex, age, indicators of parental education, maternal smoking (cigarettes per day), an indicator for gas stove, and an indicator for each of the cities. Maternal smoking was significantly associated with most symptoms (table 2). The coefficients for the respiratory symptoms investigated in the earlier report (bronchitis, chronic cough, chest illness, and persistent wheeze) were consistent with values obtained from analysis of the earlier examination (2). Asthma rates were not significantly associated with maternal smoking. Of the referent symptoms, earache was significantly associated with maternal smoking, whereas nonrespiratory illness and hay fever were not. As in the earlier examinations of these children, the presence of a gas stove was not a predictor of current respiratory symptoms. Hay fever was negatively associated with the presence of a gas stove, nonrespiratory illness was positively associated, and no association was found for earache.

The logarithm of pulmonary function was fitted to a multiple linear regression model including sex, sex-specific log of height, age, indicators of parental education, maternal smoking, an indicator for gas stove, and indicators for each city. Maternal smoking was negatively associated with all measures of lung function except FVC (table 3). For FVC and

TABLE 1

CITY-SPECIFIC AGE DISTRIBUTION OF WHITE CHILDREN IN COHORT

	10 yr	11 yr	12 yr	Total
Portage, WI	285	282	245	812
Topeka, KS	252	593	368	1,213
Watertown, MA	240	277	260	777
Kingston, TN	106	198	227	531
St. Louis, MO	283	363	350	996
Steubenville, OH	377	357	359	1,093
Total	1,543	2,070	1,809	5,422

FEV_1, the coefficients were comparable to those reported previously (2). The strongest associations were found for $FEV_{0.75}$ and MMEF, two measures not available in the earlier analysis. Because FVC was positively associated with maternal smoking, the ratios of FEV_1 and MMEF to FVC both had strong negative associations with maternal smoking.

The presence of a gas stove was negatively associated with FVC, FEV_1, and $FEV_{0.75}$. These deficits were not statistically significant, but were comparable to earlier estimates (2). MMEF and the ratio measures were positively associated with gas stove, but the associations were not statistically significant.

The city-specific symptom prevalence and pulmonary function levels, adjusted to the population distribution of the covariates described above, are given in table 4.

Associations with Air Pollutant Concentrations

City-specific annual means of the 24-h average air pollution concentrations were calculated for the 12 months preceding the examination of each child and averaged for each city (table 4). For most pollutants, the annual pollution means were lowest in Portage, Topeka, and Watertown and highest in Kingston, St. Louis, and Steubenville. Ozone concentrations, however, were highest in the communities with low concentrations of other pollutants. Except for ozone, the correlations among pairs of pollution measures varied between 0.53 and 0.98. Ozone concentrations were negatively correlated with all other pollutants, -0.96 with NO_2 and between -0.78 and -0.73 otherwise.

Results from regression of the adjusted logits of symptom frequencies on the air pollutant concentrations, expressed as the relative odds of a positive response in the most- and least-polluted city, are given in table 5. Over the range of TSP concentrations observed (34.1 to 80.0 $\mu g/m^3$) (table 4), the odds of bronchitis were estimated to increase by a factor of 2.31 with a 95% CI of 0.79 to 6.78, and similar results were obtained for PM_{15} (figure 1), $PM_{2.5}$, and FSO_4, the three other measures of particle mass. The association was statistically significant only for PM_{15}. Smaller and nonsignificant associations with bronchitis rates were found for SO_2 and NO_2. No association was found between ozone concentrations and bronchitis rates. Sex-specific regressions did not indicate any difference in response between the sexes. For example,

TABLE 2

ESTIMATED RELATIVE ODDS (95% CONFIDENCE INTERVAL) OF REPORTED SYMPTOMS VERSUS MATERNAL SMOKING AND GAS STOVES, ADJUSTED FOR SEX, AGE, PARENTAL EDUCATION AND CITY OF RESIDENCE IN CHILDREN 10 TO 12 YEARS OF AGE. SIX CITIES STUDY: 1980–1981 SCHOOL YEAR

	Mother's Smoking (1 pack/day)	Gas Stoves
Respiratory symptoms		
Bronchitis	1.28 (1.07, 1.53)	1.02 (0.77, 1.35)
Chronic cough	1.18 (0.98, 1.41)	0.88 (0.67, 1.16)
Chest illness	1.17 (1.01, 1.35)	0.97 (0.79, 1.20)
Persistent wheeze	1.20 (1.04, 1.40)	0.89 (0.71, 1.11)
Asthma	1.07 (0.85, 1.34)	0.76 (0.54, 1.05)
Reference symptoms		
Hay fever	0.92 (0.78, 1.08)	0.70 (0.56, 0.87)
Earache	1.21 (1.09, 1.35)	0.95 (0.81, 1.12)
Nonrespiratory illness	1.16 (0.94, 1.42)	1.30 (0.96, 1.76)

TABLE 3

ESTIMATED PERCENT EFFECT (95% CONFIDENCE INTERVAL) OF MATERNAL SMOKING AND GAS STOVES ON PULMONARY FUNCTION ADJUSTED FOR SEX, SEX-SPECIFIC LOGARITHM OF HEIGHT, AGE, PARENTAL EDUCATION, AND CITY OF RESIDENCE IN CHILDREN 10 TO 12 YEARS OF AGE. SIX CITIES STUDY: 1980–1981 SCHOOL YEAR

	Mother's Smoking (1 pack/day)	Gas Stoves
FVC	+0.6% (+0.1, +1.1)	−0.5% (−1.2, +0.2)
FEV_1	−0.4% (−0.9, +0.2)	−0.3% (−1.1, +0.5)
$FEV_{0.75}$	−0.7% (−1.3, −0.2)	−0.2% (−1.0, +0.6)
MMEF	−3.4% (−4.5, −2.4)	+1.0% (−0.5, +2.6)
FEV_1/FVC	−1.0% (−1.3, −0.7)	+0.3% (−0.2, +0.7)
MMEF/FVC	−3.9% (−4.9, −2.9)	+1.5% (+0.0, +3.0)

TABLE 4

CITY-SPECIFIC RATES OF SYMPTOMS, PULMONARY FUNCTION, AND 12-MONTH MEAN POLLUTION CONCENTRATIONS FOR CHILDREN 10 TO 12 YEARS OF AGE. SIX CITIES STUDY: 1980–1981 SCHOOL YEAR

	Portage	Topeka	Watertown	Kingston	St. Louis	Steubenville
Respiratory symptoms, %						
Bronchitis	3.6	6.0	4.7	10.0	6.4	8.1
Chronic cough	3.0	7.3	2.3	6.7	6.6	8.7
Chest illness	7.6	11.7	9.3	15.9	7.2	16.1
Persistent wheeze	9.6	11.4	6.8	10.6	8.9	9.6
Asthma	5.1	5.9	3.2	4.4	3.4	3.3
Reference symptoms, %						
Hay fever	20.0	22.7	12.1	23.1	32.8	23.1
Earache	10.7	12.6	10.9	6.7	12.7	5.7
Nonrespiratory illness	4.9	4.3	6.0	5.1	4.5	4.5
Pulmonary function, L						
FVC	2.556	2.492	2.511	2.487	2.511	2.539
FEV_1	2.225	2.142	2.178	2.156	2.166	2.191
$FEV_{0.75}$	2.042	1.960	2.002	1.968	1.963	2.007
MMEF	2.635	2.529	2.585	2.607	2.589	2.611
Pulmonary function ratios						
FEV_1/FVC	0.870	0.859	0.867	0.868	0.862	0.853
MMEF/FVC	1.030	1.014	1.030	1.047	1.031	1.030
Particulate pollution, $\mu g/m^3$						
TSP	34.1	63.2	53.8	63.8	80.0	71.2
PM_{15}	20.1	33.4	25.8	42.3	37.8	58.8
$PM_{2.5}$	12.7	11.8	17.7	25.7	22.0	36.7
FSO_4	4.3	3.2	5.7	7.9	7.1	13.9
Gaseous pollution, ppb						
SO_2	4.2	3.5	10.5	8.5	13.5	27.8
NO_2	6.5	12.7	19.9	15.4	22.6	22.6
O_3	37.8	30.3	22.0	25.4	23.2	18.0

Definition of abbreviations: TSP = total suspended particles; PM_{15} and $PM_{2.5}$ = particulate matter less than 15 μm and 2.5 μm aerodynamic diameter; FSO_4 = fine-fraction aerosol sulfate.

TABLE 5

ESTIMATED RELATIVE ODDS OF SYMPTOMS AND 95% CONFIDENCE INTERVAL BETWEEN THE MOST POLLUTED AND LEAST POLLUTED CITIES FOE EACH POLLUTANT UNIVARIATELY

	TSP	PM_{15}	$PM_{2.5}$	FSO_4	SO_2	NO_2	O_3
Respiratory symptoms							
Bronchitis	2.3	2.5	2.1	2.0	1.5	1.7	0.5
	(0.8, 6.8)	(1.1, 6.1)	(0.8, 5.9)	(0.6, 6.7)	(0.4, 5.8)	(0.5, 5.5)	(0.2, 1.7)
Chronic cough	3.4	3.7	2.3	2.2	1.8	1.8	0.6
	(0.7, 14.5)	(1.0, 13.5)	(0.4, 13.2)	(0.3, 15.2)	(0.3, 12.5)	(0.3, 10.5)	(0.1, 4.5)
Chest illness	1.4	2.3	2.0	1.9	1.5	1.2	0.6
	(0.3, 6.5)	(0.8, 6.7)	(0.6, 6.2)	(0.5, 6.9)	(0.4, 5.9)	(0.3, 4.6)	(0.2, 2.5)
Persistent wheeze	1.1	1.2	1.0	1.0	0.9	0.8	1.2
	(0.5, 2.5)	(0.5, 2.6)	(0.5, 2.2)	(0.4, 2.2)	(0.4, 1.9)	(0.4, 1.6)	(0.6, 2.7)
Asthma	0.7	0.7	0.6	0.6	0.6	0.6	1.9
	(0.3, 1.9)	(0.3, 2.0)	(0.3, 1.4)	(0.3, 1.4)	(0.3, 1.2)	(0.3, 0.9)	(1.0, 3.4)
Reference symptoms							
Hay fever	0.9	0.5	0.4	0.4	0.6	0.6	1.6
	(0.2, 3.6)	(0.2, 1.2)	(0.2, 0.9)	(0.2, 0.9)	(0.2, 1.7)	(0.2, 2.6)	(0.4, 6.0)
Earache	2.1	1.6	1.3	1.3	1.2	1.2	1.0
	(0.6, 7.4)	(0.4, 7.0)	(0.3, 5.6)	(0.3, 6.0)	(0.3, 5.3)	(0.3, 4.9)	(0.2, 4.7)
Nonrespiratory illness	0.9	0.9	1.0	1.0	1.0	1.0	0.9
	(0.5, 1.4)	(0.6, 1.4)	(0.6, 1.6)	(0.6, 1.6)	(0.6, 1.5)	(0.6, 1.6)	(0.6, 1.6)

For definition of abbreviations, see table 4.

the estimated odds for bronchitis versus PM_{15} was 2.48 for boys and 2.60 for girls.

Similar associations were found for chronic cough and chest illnesses. The odds of reported illness were estimated to increase by approximately a factor of two across the range of particulate exposures. Much weaker positive associations were found with SO_2 and NO_2, and a negative association with ozone.

Persistent wheeze was not associated with any of the air pollution measures. Asthma rates were negatively associated with all pollutants except ozone. A similar pattern was found for hay fever, suggesting a higher reporting among those children in the more rural communities. Asthma and hay fever rates were positively associated with annual mean ozone concentrations—estimated relative odds for asthma, 1.88 (95% CI, 1.03 to 3.43) and for hay fever, 1.62 (95% CI, 0.44 to 6.0). Of the other two reference symptoms considered, earache had a weak positive association with the particulate measures, and nonrespiratory illness had estimated relative odds very close to one for each pollutant.

Only TSP concentration was consistently associated with estimated lower levels of pulmonary function. Over the range of concentrations observed, the largest deficit, -2.7% (95% CI, -6.5 to +1.2%), was found for $FEV_{0.75}$. There was little evidence for an association between lower pulmonary function level and the annual mean concentration of any other pollutant.

Susceptible Populations

The prevalence of respiratory symptoms was much higher among the 571 children with asthma or persistent wheeze than among children without these symptoms. Bronchitis was reported among 25.5% of the children with asthma or wheeze versus 4.0% among those without; for chronic cough the rates were 29.5% versus 3.2%, and for chest illness 36.5% versus 7.6%. Although FVC was only 0.3% lower among these children with asthma
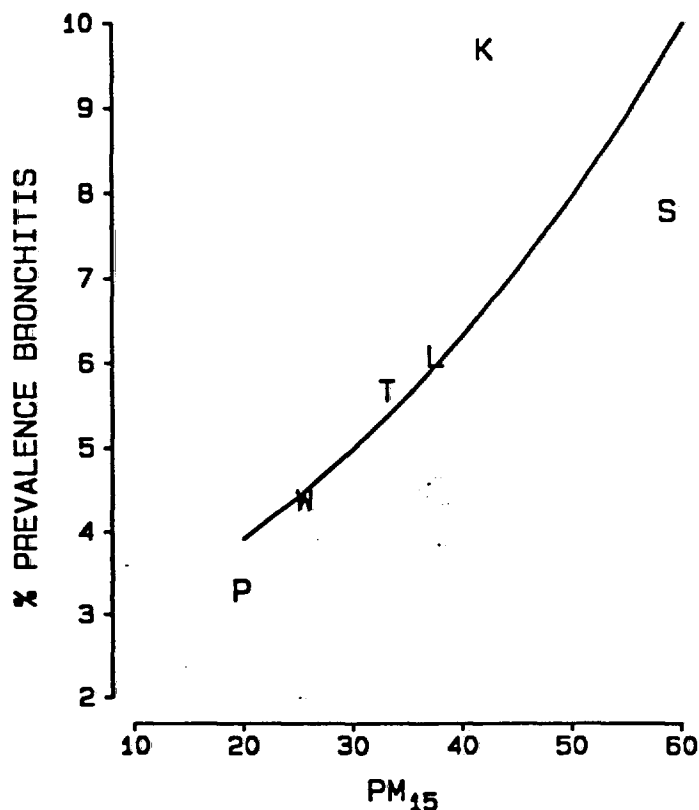

Fig. 1. City-specific prevalence of reported bronchitis versus annual mean PM_{15} concentrations ($\mu g/m^3$) and logistic fit to data (P = Portage, T = Topeka, W = Watertown, K = Kingston, L = St. Louis, and S = Steubenville).

TABLE 6

ESTIMATED RELATIVE ODDS OF RESPIRATORY SYMPTOMS AND 95% CONFIDENCE INTERVAL BETWEEN THE MOST POLLUTED AND LEAST POLLUTED CITY FOR EACH POLLUTANT, UNIVARIATELY, STRATIFIED BY REPORTED ASTHMA OR PERSISTENT WHEEZE

	Wheeze or Asthma	TSP	PM_{15}	$PM_{2.5}$	FSO_4	SO_2
Bronchitis	No	2.0 (0.9, 4.7)	2.2 (1.1, 4.2)	1.8 (0.8, 4.3)	1.7 (0.6, 4.7)	1.5 (0.5, 4.3)
	Yes	3.2 (0.6, 16.1)	3.8 (0.9, 15.5)	3.5 (0.9, 13.2)	3.1 (0.6, 16.8)	2.0 (0.3, 14.3)
Chronic cough	No	4.1 (1.6, 10.3)	4.1 (1.9, 9.2)	3.0 (0.9, 10.7)	2.9 (0.6, 13.1)	2.4 (0.5, 11.7)
	Yes	4.0 (0.2, 78.2)	5.0 (0.4, 71.6)	2.4 (0.1, 49.5)	2.4 (0.1, 60.6)	1.9 (0.1, 44.1)
Chest illness	No	1.2 (0.3, 5.4)	2.1 (0.7, 6.4)	1.9 (0.6, 5.7)	1.9 (0.6, 6.4)	1.5 (0.4, 5.6)
	Yes	2.3 (0.3, 16.7)	3.8 (1.1, 13.5)	3.1 (0.7, 12.6)	2.9 (0.5, 15.6)	1.9 (0.3, 13.0)

For definition of abbreviations, see table 4.

or wheeze, FEV_1 was 4.5% lower, $FEV_{0.75}$ was 4.3% lower, and MMEF was 10.6% lower. These children were considered as a potentially susceptible subgroup, and the associations between air pollutant concentrations and adjusted city-specific respiratory symptom rates and pulmonary function levels for children with and without these symptoms were compared.

The estimated relative odds over the range of each of the particulate measures and SO_2 is given separately for the two groups in table 6. Bronchitis rates gave relative odds of 2.2 (95% CI, 1.1 to 4.2) versus PM_{15} for children without asthma or wheeze. The estimated relative odds were higher, 3.8 (95% CI, 0.9 to 15.5), for those reporting asthma or wheeze. Children reporting asthma or wheeze not only had a higher prevalence of bronchitis, but apparently a stronger association with PM_{15} concentrations (relative odds ratio, 3.8/2.2 = 1.7; 95% CI, 0.5 to 6.3). Although this difference is not statistically significant on the logistic scale, when these results are plotted on a linear prevalence scale (figure 2), it is clear that children with asthma or wheeze were reporting most of the excess number of cases of bronchitis in the more polluted communities. Similar associations were found between bronchitis and each of the other particulate measures. The associations of bronchitis with SO_2 were smaller in magnitude than with the particulate measures, but were larger for children with asthma or wheeze than for those without (table 6). Results for chest illness in the past year were comparable to those for bronchitis, except that the SO_2 association was smaller among children with asthma or wheeze. The association between pollutant concentration and chronic cough was not stronger, however, among those with asthma or wheeze (table 6).

Separate regressions of the adjusted city-specific pulmonary function levels on air pollution for children with and without asthma or wheeze did not show any associations (figure 3).

Discussion

The first aim of these analyses was to re-examine the previously reported associations between air pollution concentrations and respiratory illness and symptom rates in the same children an average of 3 yr older, using exposure data of documented quality obtained under a standardized protocol. These reanalyses showed associations of particulate and sulfur oxide concentrations with respiratory illness and symptom rates that correspond closely to those found in the earlier analyses. Thus, these findings cannot be attributed to errors in the measurement of ambient air pollution concentrations.

In the earlier analyses (1), annual mean TSP concentrations varied between 39.3 $\mu g/m^3$ in Portage and 114.1 $\mu g/m^3$ in Steubenville. This range was associated
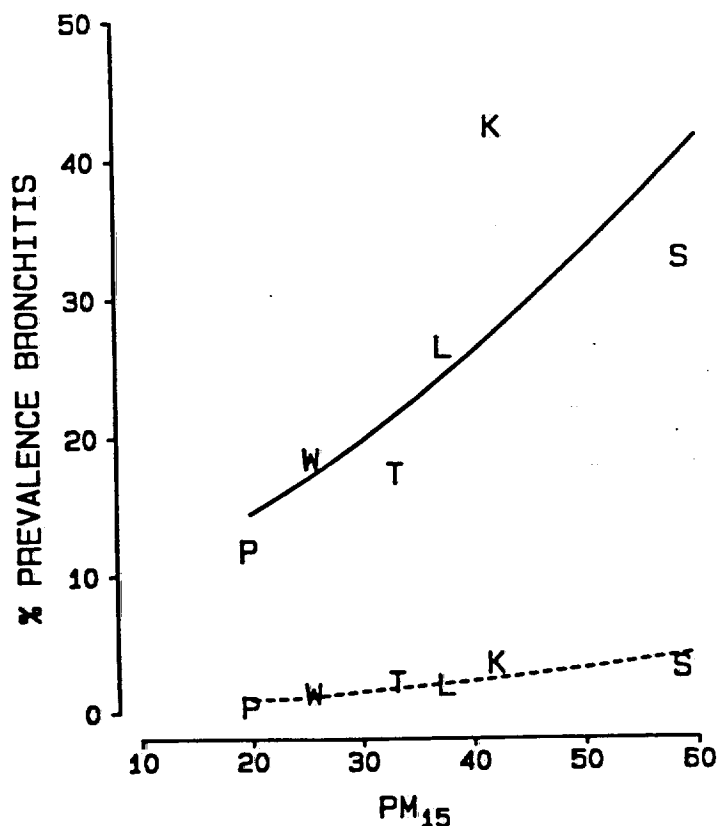

Fig. 2. City-specific prevalence of reported bronchitis versus annual mean PM_{15} concentrations ($\mu g/m^3$) stratified by reported asthma or persistent wheeze. Upper curve (solid line) is the logistic fit for children with reported asthma or wheeze, and lower curve (dashed line) is the logistic fit for those without (see figure 1 for city labels).
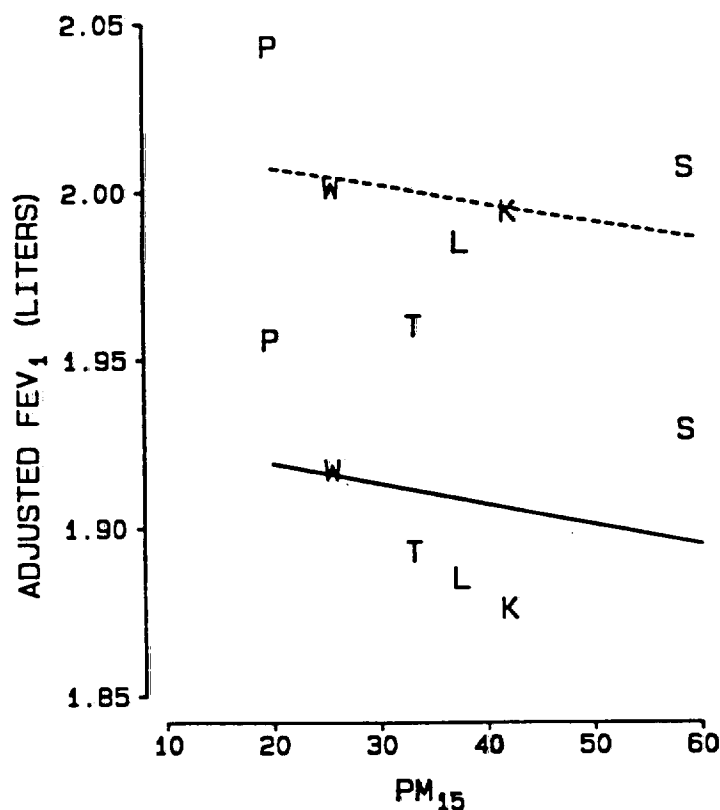
Fig. 3. City-specific adjusted FEV₁ versus annual mean PM₁₅ concentrations (μg/m³) stratified by reported asthma or persistent wheeze. Lower curve (solid line) is the linear fit for children with reported asthma or wheeze, and upper curve (dashed line) is for those without (see figure 1 for city labels).

with a between-cities relative odds for chronic cough of 2.13 with a 95% CI of 1.63 to 2.77. Similarly, the relative odds were 2.13 (95% CI, 1.08 to 4.18) for bronchitis, 1.34 (95% CI, 0.70 to 2.55) for chest illness, and 1.23 (95% CI, 0.76 to 7.00) for persistent wheeze. Despite a decline in the TSP concentrations in the most polluted cities, Steubenville and St. Louis, between the first two examinations in the 1975 to 1977 school years and the 1980-1981 school year, the estimated relative odds obtained in the current analysis are comparable to those obtained earlier. The estimated relative odds for the referent symptoms of hay fever and nonrespiratory illness were not elevated. A positive association was found between earache and particulate pollution, although the association was far from statistical significance. This is consistent with the increased prevalence of earache associated with maternal smoking (table 2).

The differences in respiratory illness reporting between cities may represent differences in the samples of children that are unrelated to air pollution exposure.

Those cities visited in the spring have been noted to have both higher rates of respiratory symptom reporting and higher air pollution values. Hence, the positive associations may be attributable in part to better recall of symptoms in the previous winter when questionnaires were administered in the spring compared with those administered in the fall. When season of examination was included in the regression analyses, the estimated relative odds of symptom reporting were reduced. For example, the estimated effect of PM₁₅ on reported bronchitis was reduced from 2.52 (table 5) to 1.97 when adjusted for season. Other potential confounders include differences in interpretation of the questionnaire by the respondent and persistent differences in illness or reporting rates associated with ethnic or cultural factors.

The city-specific symptom reporting rates and adjusted level of pulmonary function have been shown to be consistent within each city year to year (1). However, the variability of these summary measures between cities was larger

then the random fluctuation between individuals would predict. Because of this clustering effect in the data, two-step methods were used to analyze the health outcomes. The effect of these methods is to produce conservative estimates of the statistical significance of the reported associations compared with commonly used methods. For example, if bronchitis were regressed on PM₁₅ exposure for each child, adjusting for covariates in a logistic model, a highly significant positive association is found (p = 0.000024). Using the two-step method, bronchitis had a marginally significant positive association with PM₁₅ (p = 0.016). The estimated odds ratios are similar in both cases. The confidence intervals presented here reflect this adjustment for the clustering of response within city.

In the previous report, data from 3 yr were considered in each city, and three of the cities (Kingston-Harriman, St. Louis, and Steubenville) were divided into two exposure regions based on topography, local sources of pollutants, and air pollution measurements from multiple monitors. This permitted evaluation of the covariance of health status and air pollution within cities. By 1980, there was no evidence for spatial differences in exposure within Kingston-Harriman or St. Louis. The air monitor in Steubenville was located centrally, at a location intermediate between the two previously defined air pollution regions. Thus, the data from the 1980-1981 school year did not allow investigation of the spatial or temporal covariation of air pollution and respiratory health within cities.

The second aim was to investigate the effects of pollutants other than TSP, SO₂, and SO₄, particularly measures of fine particulate air pollution. Because data were available for only six cities, however, the information differentiating pollutants is somewhat limited. Each pollutant was therefore considered univariately, and multivariate comparisons were not attempted.

All of the particulate measures, TSP, PM₁₅, PM₂.₅, and FSO₄, are highly correlated across the six cities. All are associated with substantial increases in the reported rates of respiratory illnesses over the range of annual means observed. Each of these particulate measures has well-known limitations (12, 13). TSP has a poorly defined upper size cut that depends on wind speed and direction. PM₁₅ may underestimate exposure because of coarse particle loss in shipping (14). PM₂.₅ is lightly contaminated by less than absolute separation of particles at 2.5 μm.

The FSO_4 concentration may overestimate sulfur concentrations slightly because of conversion of SO_2 to SO_4 on the filter and the assumption that all sulfur is SO_4.

Of the particulate measurements, only associations with PM_{15} were statistically significant. Dzubay and Barbour (14) have reported a loss of between 19 and 53% of coarse particle mass from filters during shipping between the sample site and the laboratory. The potential variable loss of coarse particles in shipping and handling would normally cause concern about the validity of the associations with PM_{15}. However, starting late in 1980, independent measurements of PM_{15} were made by high-volume samplers with sampling heads that removed particles with an aerodynamic diameter greater than 15 μm. The annual mean concentrations for 1981 from these samplers were 22.8 μg/m³ in Portage, 37.6 μg/m³ in Topeka, 29.8 μg/m³ in Watertown, 41.5 μg/m³ in Kingston, 44.3 μg/m³ in St. Louis, and 62.6 μg/m³ in Steubenville. Comparison with PM_{15} concentrations (table 4) shows that the inhalable particulates were higher by an average of 3.4 μg/m³ and the correlation between the annual means was 0.98. Thus, any bias in the PM_{15} caused by shipping losses in these samples must be small. Moreover, such randomly variable error in the exposure measurement would only underestimate the true association.

Bronchitis and chest illness rates were noted to be higher in Kingston than in any of the other cities, including Steubenville, which has the highest particulate pollution concentrations. Lippmann (15) has suggested that these higher respiratory illness rates may be due to the acidity of the suspended particles in Kingston and Steubenville. Acidity measurements were not made in 1980 or 1981, but recent measurements have shown that aerosol acidity is in fact higher in Kingston and Steubenville (16).

Sulfur dioxide, which is also correlated with the particulate measures, has a much weaker association with the respiratory symptoms than the particulate measures. Similar results were found in the earlier study. Nitrogen dioxide annual means are higher in the more urbanized cities (Watertown and St. Louis) and the industrial city (Steubenville) than in the more rural cities (Portage, Topeka, and Kingston). The association of NO_2 with respiratory symptoms, however, was weak.

Ozone concentrations were highest in the most rural community (Portage).

Ozone is a secondary pollutant formed by photochemical reactions as polluted air masses move away from the pollution source regions. Primary pollutants such as nitric oxide (NO) rapidly scavenge O_3, converting it to molecular oxygen and the NO to NO_2. Thus, ozone levels tend to be low in regions that are sources of these primary pollutants such as Steubenville, St. Louis, and Watertown and high in more pristine areas such as Portage, Topeka, and Kingston. Negative associations of respiratory symptoms with ozone probably do not represent a protective effect of ozone, but rather indicate the negative correlation between ozone and other pollutants.

The third aim was to test for associations between air pollution and tests of pulmonary function potentially more sensitive than the previously reported FVC and FEV_1. Although $FEV_{0.75}$ and MMEF were more strongly associated with maternal smoking than were FVC or FEV_1, there was still no indication of chronic effects of air pollution on any measure. Lippmann and Lioy (12) has suggested that these chronic effects may be masked by acute changes in pulmonary function associated with exposure on the days or hours immediately before the examination. The annual pulmonary function data are being analyzed to evaluate such acute effects, and will be reported separately.

The analyses were repeated with stratification on reported asthma or persistent wheeze. Although children with reported asthma or persistent wheeze made up only about 10% of the sample, they accounted for approximately half of the children reporting chronic respiratory symptoms. Thus, stratifying by reported asthma or wheeze removes a substantial source of variability in illness and symptom responses. The separate regressions permit comparisons of the air pollution associations in the two groups of children. Positive associations were found between bronchitis, chronic cough, and chest illness and the particulate measures for both groups. The estimated relative odds of bronchitis and chest illness for the particulate measures was approximately twice as large for those with asthma or wheeze, although these differences were not statistically significant. In absolute terms, the adjusted bronchitis rate for children without asthma or wheeze increased from 2.4% in Portage to 5.2% in Steubenville, a rate difference of 2.8% (see figure 2). For children with asthma or wheeze, the adjusted bronchitis rate increased from 13.7%

in Portage to 34.7% in Steubenville, a rate difference of 21.0%. Thus, the smaller group of children that reported asthma or wheeze contributes to most of the cases of bronchitis that could be attributed to air pollution.

In summary, these analyses provide further evidence that there is an increase in respiratory symptom reporting across the six cities that is associated with annual mean particulate levels in these communities. Stronger associations were found with concentrations of inhalable particles, PM_{15}, although the power to differentiate the effects of specific size ranges was weak. Unexplained differences in symptom reporting between cities may be explained by specific components of the particle exposure not considered, e.g., aerosol acidity. Such associations are being investigated in later follow-up examinations of these and other cohorts of children.

Children with reported persistent wheeze or asthma were found to have substantially higher reporting rates for respiratory illnesses and lower pulmonary functions. The proportion of these children within the sample varies between communities. In the more polluted communities, a large fraction of these children are reporting respiratory symptoms. Thus, these children appear to be reacting more in response to air pollution exposure than the rest of the sample. Controlled exposure studies of adolescent asthmatics (17) have suggested that such children may be especially responsive.

There was no evidence for an effect of pollution exposure on level of pulmonary function, either in the complete cohort or in the children with reported persistent wheeze. Thus, air pollution exposure may increase respiratory symptom rates without causing irreversible pulmonary function losses. Nevertheless, although respiratory symptoms may be transient, they clearly have health consequences of some importance. In particular, respiratory illness in childhood has been reported as a risk factor for the subsequent development of respiratory diseases in adulthood and also a risk factor for the development of COPD in smokers (18). Longitudinal analysis of data provided by these children as they pass through adolescence may provide additional information about the long-term effects of these pollutant exposures.

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Kauffmann, F., Tager, I.B., Munoz, A., Speizer, F.E. "Familial
Factors Related To Lung Function In Children Aged 6-10 Years"
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ABSTRACT. Familial factors related to lung function between six
and 10 years of age have been studied among 1,160 children whose
both parents were examined in 1975 in the French PAARC (Pollution
Atmospherique et Affections Respiratoires Chroniques) Cooperative
Study. The three indices FVC (forced vital capacity), FEV1 (forced
expiratory volume in one second), and FEF25-75 (forced expiratory
flow between 25 and 75 per cent of the vital capacity) were studied
after adjustment for sex, town, age, and height (and weight for
children's FVC and FEV1). Maternal (but not paternal) smoking was
associated with a significant decrease in FEV1 and FEF25-75, but
not in FVC. Familial resemblance was observed for all indices
between children and parents and between siblings. None of the
environmental factors considered (i.e.,parental smoking or
education) or body habitus explained the familial resemblance
observed. Conversely, after taking into account the aggregation
between siblings, associations between children's lung function
and parental characteristics (smoking, lung function) remained
signficant. Parental-children correlations exhibited an increasing
temporal trend with increasing age of the children. All but one
correlation for FVC, FEV1, and FEF25-75 residuals of children with
mothers' residuals were higher in the oldest age group compared
with they youngest age group at the 0.10 level. Furthermore,
correlations between siblings of opposite sex were significantly
lower than correlations between siblings of like sex, especially
for FEV1/FVC and FEF25-75/FVC. Results suggest that different
growth patterns between boys and girls may be a critical factor in
the study of lung function familial resemblance.

FAMILIAL FACTORS RELATED TO LUNG FUNCTION IN CHILDREN AGED 6-10 YEARS

RESULTS FROM THE PAARC EPIDEMIOLOGIC STUDY

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Kauffmann F. (INSERM U. 169, 16 ave. PV Couturier, F-94807 Villejuif Cédex, France), I. B. Tager, A. Muñoz, and F. E. Speizer. Familial factors related to lung function in children aged 6-10 years: results from the PAARC epidemiologic study. *Am J Epidemiol* 1989;129:1289-99.

Familial factors related to lung function between six and 10 years of age have been studied among 1,160 children whose both parents were examined in 1975 in the French PAARC (Pollution Atmosphérique et Affections Respiratoires Chroniques) Cooperative Study. The three indices FVC (forced vital capacity), FEV$_1$ (forced expiratory volume in one second), and FEF$_{25-75}$ (forced expiratory flow between 25 and 75 per cent of the vital capacity) were studied after adjustment for sex, town, age, and height (and weight for children's FVC and FEV$_1$). Maternal (but not paternal) smoking was associated with a significant decrease in FEV$_1$ and FEF$_{25-75}$, but not in FVC. Familial resemblance was observed for all indices between children and parents and between siblings. None of the environmental factors considered (i.e., parental smoking or education) or body habitus explained the familial resemblance observed. Conversely, after taking into account the aggregation between siblings, associations between children's lung function and parental characteristics (smoking, lung function) remained significant. Parental-children correlations exhibited an increasing temporal trend with increasing age of the children. All but one correlation for FVC, FEV$_1$, and FEF$_{25-75}$ residuals of children with mothers' residuals were higher in the oldest age group compared with the youngest age group at the 0.10 level. Furthermore, correlations between siblings of opposite sex were significantly lower than correlations between siblings of like sex, especially for FEV$_1$/FVC and FEF$_{25-75}$/FVC. Results suggest that different growth patterns between boys and girls may be a critical factor in the study of lung function familial resemblance.

child; education; growth; lung diseases, obstructive; tobacco smoke pollution

A number of epidemiologic studies have sought to investigate the influence of genetic and environmental factors on levels of lung function in children (1-6). All these

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studies have failed to adjust the statistical inferences for the nonindependence of the measurements of lung function that arises from the familial structure of the data (7). None of the studies have evaluated how different patterns of growth of lung function in children of both sexes (8) might influence the magnitude of the familial correlations observed.

In the current study, a subset of the PAARC (Pollution Atmosphérique et Affections Respiratoires Chroniques) survey (9) was used to investigate the influence of familial (genetic and environmental) factors on various measures of level of lung function (forced vital capacity (FVC), forced expiratory volume in one second (FEV_1), and forced expiratory flow between 25 and 75 per cent of the vital capacity (FEF_{25-75}) in children. The analysis uses a multivariate analytic technique (10) that permits both adjustments for the familial structure of the data and for covariates that might influence levels of function. Furthermore, a detailed analysis has been included that evaluates the effect of different patterns of lung growth in children on the observed familial correlations.

MATERIALS AND METHODS

The full data set of the French Cooperative Study PAARC includes 13,383 French households, each of which was headed by a nonmanual worker who resided for at least three years in one of 24 areas in seven French cities. The primary purpose of the larger study was to investigate the potential role of air pollution in the occurrence of respiratory symptoms and alterations in levels of pulmonary function in adults and children. The full protocol has been published elsewhere (9, 11).

Only adults aged 25–59 years (n = 20,246) and children aged 6–10 years (n = 2,979) were selected for the present study. From the full sample, a subset of 945 families, each of which included two parents and at least one child aged 6–10 years (n = 1,160: 557 girls and 603 boys), was selected for the present analysis on familial factors. The sample included 751 families with one child, 174 with two children, 19 with three children, and one with four children.

Subjects were interviewed at home by a questionnaire derived from the British Medical Research Council/European Coal and Steel Community (BMRC/ECSC) (12) questionnaire. Parental smoking history was recorded through interviews with both parents. With respect to maternal educational level, families were classified into two groups—those who completed the primary level of schooling (low) and those who completed the secondary level or who obtained a university degree (high). Lung function was evaluated with a dry expirograph (Vitalograph, Buckingham, United Kingdom) performed on 95 per cent of the adults and 92 per cent of the children interviewed. At least three forced expirations were performed in accordance with ECSC recommendations (13). The FVC and forced FEV_1 expressed at ambient temperature, pressure, and water conditions were used for analysis. Measurements were made indoors with average temperatures ranging between 12 C and 30 C (with 98 per cent between 17 C and 25 C). In addition, the FEF_{25-75} of the time-volume curve was obtained from the curve with the largest FEV_1.

Seventy-eight per cent of the adults and 70 per cent of the children in the sample provided acceptable forced time-volume curves. Inadequate performance of the pul-

monary function test was associated with lower levels of maternal education in both adults and children and with younger age among children. All subjects included in the present analysis provided acceptable forced time-volume tracings.

All measures of lung function were adjusted by means of regressions on age and height (14). They were calculated separately for adults and children by sex and by town, because there were discrepancies in the percentage of poor tracings and regression coefficients on age between towns. For children, weight was included in the regressions for FVC and FEV_1. After the adjustments, sex-specific normalized residuals were obtained for each measure of lung function according to the following:

Residual =

(observed level −

$(a_i \text{ Age} + b_i \text{ Height} + c_i))/\sqrt{s_i^2}$,

where i refers to ith town, a_i is the regression coefficient for age, b_i is the regression coefficient for height, c_i is the constant term (a coefficient for weight appears for children for FEV_1 and FVC), and s_i^2 is the residual variance. Linear regressions were used because it has been shown that over ages 6–10 years, the pulmonary function test is approximately linear with age (15), and little improvement of the multiple correlation coefficients (R^2) was obtained with more sophisticated models. Correlation coefficients for the regression of FVC (FEV_1) on age, height, and weight were 0.450 (0.401) for boys and 0.584 (0.493) for girls. Adding age^2 and $height^2$ terms only increased R^2 to 0.455 (0.404) and 0.588 (0.493), respectively. For FEF_{25-75}, correlation coefficients were much lower for boys ($R^2 = 0.14$) and for girls ($R^2 = 0.20$). These residuals are therefore adjusted for (weight) height, age, and town. For parents, height, age, town, and smoking residuals were computed by regression of the previous residuals on current cigarette tobacco use (g/day). These smoking-adjusted residuals also were normalized (mean ± standard deviation = 0 ± 1) to facilitate comparisons of associations with the different measures of lung function. The independence of the residuals used with age, height, weight, and, when appropriate, smoking was checked by careful examination of residuals plots. If a genetic factor exists, the correlations between children and the midparent (fictional subject to whom is attributed the mean value of both parents) should be the strongest. Residuals of midparents were computed as the mean of father and mother residuals. Air pollution varied according to the 24 areas and the seven cities (9). Since the primary purpose of the present analysis was to investigate the resemblance of town-adjusted lung function residuals of various household members exposed to the same pollution, air pollution will not be considered in the present report

Correlations of lung function between household members were evaluated by the adjusted pairwise correlated method of Rosner (16). This method permits the full use of all household members to compute the correlations between parents and children, while adjusting the test of significance for the intraclass correlations between siblings, i.e., for the nonindependence of the observations within a given household. A multivariate extension of this method (10) permitted adjustment of regression coefficients for the intraclass correlations among household members (especially siblings). Furthermore, it allows adjustment of intraclass correlations for various variables (such as environmental family characteristics).

Tests of statistical significance of familial correlations were one-sided, since the alternative hypothesis was that correlations between parents and children or between siblings were positive and not just different from zero (17). All other tests of significance were two-sided. In the multivariate analyses of correlations, differences in interclass correlations were evaluated by the introduction of the appropriate interaction terms in the models.

TABLE 1

Characteristics of sample of 945 households with two parents and one child,
the French Cooperative Study PAARC

	Mothers (n = 945)	Fathers (n = 945)	Girls (n = 557)	Boys (n = 603)
Age	36.5 ± 5.9*	38.9 ± 6.4	8.8 ± 1.4	8.8 ± 1.4
Height (m)	1.62 ± 0.05	1.73 ± 0.06	1.29 ± 0.10	1.30 ± 0.09
Weight (kg)	56.2 ± 7.9	72.1 ± 9.5	27.3 ± 6.1	27.7 ± 5.4
Body mass index (weight (kg)/height (m)²)	21.5 ± 2.8	24.1 ± 2.8	16.1 ± 2.1	16.2 ± 2.0
Ponderal index (height (m)/³√weight (kg)³)	42.3 ± 1.8	41.7 ± 1.7	43.3 ± 2.0	43.3 ± 1.9
FVC (liter)	3.29 ± 0.54	4.47 ± 0.75	1.73 ± 0.42	1.84 ± 0.43†
FEV₁ (liter)	2.68 ± 0.53	3.60 ± 0.71	1.50 ± 0.40	1.61 ± 0.40†
FEF₂₅₋₇₅ (liter/sec)	2.97 ± 1.02	3.82 ± 1.34	1.92 ± 0.79	1.99 ± 0.75
FEV₁/FVC	0.814 ± 0.093	0.804 ± 0.084	0.867 ± 0.105	0.872 ± 0.089
FEF₂₅₋₇₅/FVC	0.906 ± 0.284	0.856 ± 0.275	1.12 ± 0.39	1.09 ± 0.37

* Mean ± standard deviation.

† Comparison between boys and girls (t test), $p < 0.001$.

RESULTS

The general characteristics of the study population are presented in table 1. Parents were relatively young, with a two-year difference between fathers and mothers. Girls had significantly lower values than boys for FEV_1 and FVC but not for FEF_{25-75} or for the ratios FEV_1/FVC and FEF_{25-75}/FVC.

The correlations for FVC, FEV_1, and FEF_{25-75} between children and parents and between spouses were significant (table 2). Correlations between children and mothers were higher than those between children and fathers, but statistical comparison was not possible because the data are not independent. Midparent-children correlations were similar to mother-children correlations. All intraclass correlations between siblings were significant.

Tobacco smoking by parents had the expected effect of decreasing their own measures of lung function (except FVC (table 3)). The strongest effects were observed for FEF_{25-75} in mothers and FEV_1 and FEF_{25-75} in fathers.

Significant effects of maternal smoking in all measures of lung function in children (except FVC) also were observed (table 3); the strongest effects were observed for FEF_{25-75}. Intraclass correlations were only slightly decreased after taking into account maternal smoking (table 3). Paternal smoking showed virtually no effect on level of function in children (table 3).

The above data suggest that maternal tobacco smoking might partially explain patterns of familial correlations observed in table 2, i.e., maternal-children correlations greater than paternal-children correlations for FVC, FEV_1, FEF_{25-75} and midparent correlations closer to maternal correlations for these same measures. Restriction of the analysis to those families in

TABLE 2

Familial correlations of lung function residuals,
French Cooperative Study PAARC; 945 families,
1,160 children*

	FVC	FEV₁	FEF₂₅₋₇₅
Between children and parents			
Mothers	0.26*	0.26	0.21
Midparents†	0.29	0.27	0.23
Fathers	0.19	0.15	0.16
Between spouses	0.18	0.20	0.23
Between siblings	0.30	0.34	0.27

* See Materials and Methods. All correlations between children and parents (adjusted pairwise test (16)), between spouses, and between siblings are significant at the 0.001 level (one-sided).

† Midparent residuals are the mean of father and mother residuals.

TABLE 3

Effect of parental smoking on lung function level and resemblance between siblings. French Cooperative Study PAARC†

	FVC	FEV₁	FEF₂₅₋₇₅
Maternal smoking‡			
Mothers' lung function§ (smoking (g¶/day))	−0.003	−0.013*	−0.024***
Children's lung function (smoking (g/day))	−0.002	−0.010*	−0.015**
Intraclass correlation (r)‖	0.30	0.33	0.26
Paternal smoking‡			
Fathers' lung function§ (smoking (g/day))	−0.015***	−0.019***	−0.018***
Children's lung function (smoking (g/day))	−0.001	−0.003	−0.004****
Intraclass correlation (r)‖	0.30	0.33	0.27

† The method used gives adjusted regression coefficients for the intraclass correlations and adjusted intraclass correlations for the variables included in the regression (10).

‡ Eleven per cent of the mothers were current smokers (11 ± 8 g/day); 58 per cent of the fathers were current smokers (17 ± 10 g/day).

§ Regression coefficients derived from regressions of parental smoking on height-, age-, town-, and (where appropriate) weight-adjusted residuals of lung function of parents and children.

‖ All intraclass correlations between siblings are significant at the 0.01 level.

¶ Grams of tobacco.

* $p < 0.05$.

** $p < 0.01$.

*** $p < 0.001$.

**** $p < 0.10$.

which mothers never smoked (whether or not the father was a current smoker) had little effect on the pattern of parent-child correlations observed in table 2 (data not shown). Similar results were obtained when the height-, age-, and town-adjusted residuals of the parents' function also were adjusted for their current smoking by regression analysis and when these adjusted values were used to compute the parent-children correlations. Inclusion of the body build index of either the parents or children in the analysis did not alter the observed correlations between children's lung function residuals and parental lung function residuals. The familial resemblance was not abolished by looking within height/³√weight (ponderal index) or weight/height² (body mass index) parental quintiles.

Maternal working status was investigated as an indirect measure of the mothers' contact time with their children. Among families with mothers who never smoked, 264 children had mothers who had never worked, 230 had mothers who had worked in the past, and 334 had mothers who were currently working. For FEF₂₅₋₇₅,

a trend was observed in the magnitude of the maternal-children correlations: 0.29, 0.18, and 0.08 for mothers who had never worked, mothers who had worked in the past, and currently employed mothers, respectively. The difference in the correlations for mothers who had never worked and those currently working was significant ($p < 0.01$), based on the significance of the interaction term (current work • mother's FEF₂₅₋₇₅ residual) in the regression of children's FEF₂₅₋₇₅ residuals on the following variables: mother's FEF₂₅₋₇₅ residual, current work (yes = 1, other = 0), past work (yes = 1, other = 0), current work • mother's residual, and past work • mother's residual. A nonsignificant trend was observed for FEV₁, and no trend was observed for FVC.

The influence of sociocultural factors on the correlations of lung function between parents and children was investigated through the evaluation of the effects of parental education on these correlations. In general, levels of lung function were lower for parents and children in households with the least educated mothers (table 4). Intraclass correlations between sib-

TABLE 4

Effect of educational level on lung function level and resemblance between siblings, 681 families with nonsmoking mothers, 828 children, French Cooperative Study PAARC†

Mean lung function residuals	FVC	FEV_1	FEF_{25-75}
Mothers' lung function			
Primary education vs. high‡	-0.15^*	-0.14^{****}	-0.14^{****}
Fathers' lung function§			
Primary education vs. high‡	-0.25^{**}	-0.27^{**}	-0.16^*
Children's lung function			
Mother's primary education vs. high‡	0.09	-0.01	-0.11
Intraclass correlation (r) between siblings	0.29	0.34	0.24

† The method used gives adjusted regression coefficients for the intraclass correlations and adjusted intraclass correlations for the variables included in the regression (10).
‡ Regression coefficients derived from regressions of education (high = 0, primary = 1) on residuals of lung function of parents and children (see Materials and Methods); 366 mothers and 323 fathers had a primary level of education.
§ All intraclass correlations are significant at the 0.001 level.
* $p < 0.05$.
** $p < 0.01$.
**** $p < 0.10$.

lings remained significant, after adjustment for maternal educational level. Within strata of maternal education, all correlations between mothers and children remained significant, and, with the exception of FEF_{25-75}, correlations between fathers and children were also significant.

Sex of the children did not have a consistent influence in parent-children correlations, although the correlations between girls and fathers were consistently higher than those between boys and fathers.

When the sibling correlations were computed taking into account the sex composition of the sibships, considerable variability was observed (table 5). Correlations between brothers were substantially higher than those between sisters for FEF_{25-75}. The correlation for FVC was significantly higher between sisters than between other siblings, and that for FEV_1 was comparable between brothers and sisters. In opposite-sex sibships, correlations were consistently lower than for like-sex sibships (except for FVC); differences were significant between the correlations for brothers and for opposite-sex siblings. These results suggest that sex-specific growth patterns were an important factor in the pattern observed for the correlations.

Figure 1 presents the relation between FVC, FEV_1, and FEF_{25-75} and age and height for girls. FEV_1 and FVC have a roughly linear relation with height. FEF_{25-75} appears to increase nonlinearly, with a spurt beginning at about eight years of age. For boys (figure 2), all measurements of function appear to grow in an approximately linear fashion until age 10, when there appears to be a further increase in FEF_{25-75} without an accompanying change in FEV_1 and FVC.

The ratios FEF_{25-75}/FVC and FEV_1/FVC, potential measures of "dysanapsis," that is, of the unequal growth of lung airways and parenchyma, were evaluated. Sibling correlations for the ratios (0.18 for FEV_1/FVC and 0.14 for FEF_{25-75}/FVC) were lower for these indices than were the correlations observed for FVC, FEV_1, or FEF_{25-75} (table 2). Similarly, for opposite-sex sibships, there was virtually no intraclass correlation for FEF_{25-75}/FVC. To further explore the relations noted in figures 1 and 2, regressions of FEV_1/FVC and FEF_{25-75}/FVC on height were carried out for seven different age-sex categories (figure 3). For males, the coefficients for height for FEF_{25-75}/FVC, and to a lesser extent for FEV_1/FVC, had significantly negative values up to the age range 87-96 months. Although only one of the regression coeffi-

TABLE 5

Intraclass correlations of lung function residuals, by sex of the siblings, French Cooperative Study PAARC

	FVC	FEV₁	FEF₂₅₋₇₅	FEV₁/FVC	FEF₂₅₋₇₅/FVC
Brothers (B) (n = 50)†	0.23‡	0.39	0.41	0.27	0.32
Sisters (S) (n = 48)	0.45	0.41	0.25	0.13	0.16
Opposite-sex sibs (BS) (n = 112)	0.21	0.25	0.20	0.11	0.01
Comparison§					
BS-B				*	**
BS-S	**				
B-S	****				

† Number of sibships.

‡ All correlations except sisters FEV_1/FVC ($p < 0.10$) and opposite sex FEF_{25-75}/FVC are significant at the 0.05 level.

§ Fisher's z test.

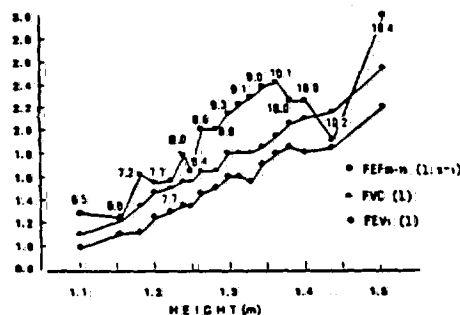* $p < 0.05$.
** $p < 0.01$.
**** $p < 0.10$.

FIGURE 1. Lung function according to height and age for 557 girls, French Cooperative Study PAARC. Height was divided into 18 categories of approximately equal numbers of girls. Lung function values plotted are the median values of each height category, and median age values are figured on the graph. FVC and FEV₁ are expressed in liters, FEF₂₅₋₇₅ in liters per second.

FIGURE 2. Lung function according to height and age for 603 boys, French Cooperative Study PAARC. Height was divided into 18 categories of approximately equal numbers of boys. Lung function values plotted are the median values of each height category, and median age values are figured on the graph. FVC and FEV₁ are expressed in liters, FEF₂₅₋₇₅ in liters per second.

cients for height was significantly different from zero for girls (age range 96–105 months, $p = 0.07$), all were positive until ages 114–123 months. If height is taken as an index of growth, the negative coefficients for males indicate that over the entire age range studied, but especially up to the range of 96–105 months, FEF₂₅₋₇₅ is growing at a slower rate than FVC.

The effect of the above differences in growth of lung function on the familial correlations is presented in table 6. Among girls, the correlations with maternal lung function increase in the age group 96–114 months for FVC and FEF₂₅₋₇₅. In the same

age group, there is an increase in the correlations with fathers' FVC and FEV₁. Among boys, the increase in the correlation with mothers' lung function occurs in the oldest group (>114 months) for FVC; the increase in the correlation with maternal lung function occurs in the middle age group (96–114 months) for FEF₂₅₋₇₅.

DISCUSSION

The present investigation focuses on the factors that contribute to familial resemblance in lung function as observed in a

population-based cross-sectional study. As in previous investigations (1-3), familial resemblance has been observed, and the magnitude of the resemblance is similar to published results. In contrast to past investigations, the current work has made a detailed study of the extent to which a wide

variety of intrinsic (e.g., age, sex, height, patterns of growth of lung function in children), environmental (e.g., parental smoking), and sociocultural (e.g., parental education) factors might be responsible for the familial resemblance observed. These factors have been taken into account in the analysis of the familial structure of the data.

The performance of an unacceptable tracing among children was associated with younger age, reported by others (18), and to a low maternal educational level. Familial resemblance in lung function was studied for age-adjusted indices and persisted after taking educational level into account. Therefore, exclusion of subjects with unacceptable tracings is unlikely to have seriously biased the estimation of the resemblance.

The extent to which familial resemblance in lung function is primarily a reflection of the tendency for family members to have a similar body habitus has been a source of controversy (2). Lebowitz et al. (6) did not observe aggregation of pulmonary function after adjustment for ponderal index (height/$^3\sqrt{}$weight). Body habitus (ponderal index or body mass index) did not affect the magnitude of the parental-children correlations for FVC, FEV_1, or FEF_{25-75} in the present work.
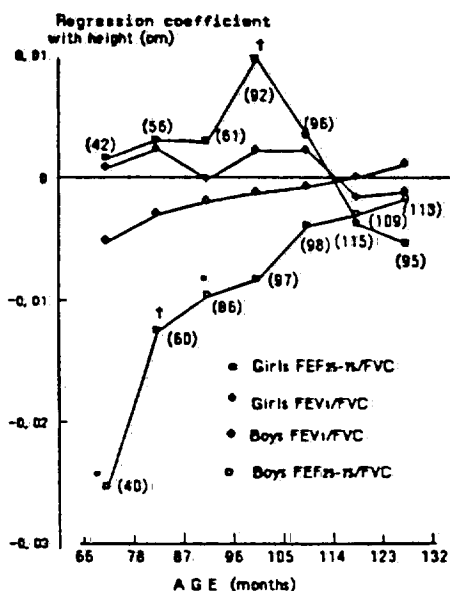
A factor that might account for some of

FIGURE 3. Sex-specific dysanaptic growth, French Cooperative Study PAARC. Dysanaptic growth refers to a disproportionate growth of airways and parenchyma. $*$, $p < 0.05$; $\dagger$, $p < 0.10$.

TABLE 6

Correlations of adjusted lung function residuals between parents and children, by sex and age of the children, French Cooperative Study PAARC*

Sex and age (months)	FVC		FEV_1		FEF_{25-75}	
	Mothers	Fathers	Mothers	Fathers	Mothers	Fathers
Girls						
66-95 (n = 159)	0.14	0.10†	0.26	0.04†	0.13	0.15
96-114 (n = 188)	0.30	0.22	0.30	0.21	0.28	0.13
115-132 (n = 210)	0.28	0.22	0.21	0.22	0.30	0.23
Boys						
66-95 (n = 186)	0.18	0.14	0.17	0.17	0.07†	0.13
96-114 (n = 195)	0.13	0.20	0.25	0.10†	0.20	0.15
115-132 (n = 222)	0.41	0.18	0.33	0.11†	0.23	0.12

* All correlations of children with mothers' residuals in the oldest age group were higher, at least at the 0.10 level, than correlations in the youngest age group, except for FEV_1 among girls, for whom the increase in correlation coefficients was significant with fathers' values (Fisher's r test).

† Not significant at the 0.05 level (one-sided test).

the divergence in the results related to body size is the different pattern of growth in lung function observed between boys and girls. Different patterns of airway-parenchymal-somatic growth relations in the two sexes have already been described by Pagtakhan et al. (19). They reported that among girls a rapid growth of smaller airways which outgrows lung development during somatic growth seems to occur before puberty. In the present study, as indicated in figures 1–3, girls aged 6–10 years showed a pattern of increase in lung function measurements characterized by a more rapid growth rate in flows (FEF_{25-75}) relative to volumes (FEV_1, FVC) up through ages 8.75 years, with a "spurt" in flow growth at about age eight years. Such mid-growth spurt has already been noticed for various indices such as height (20) or chest circumference (21). In contrast, boys showed growth of FEF_{25-75} that was relatively slower than that observed for volumes, but which progressively increased over the age range 6–10 years (figure 3). When parent-child correlations were calculated for the different growth stages of the children, increases were observed in the correlations, particularly for maternal-child correlations. Such temporal variation in familial resemblance is well known during the pubertal spurt for factors markedly genetically determined, such as height (22). Failure to take into account the heterogeneity in the parent-children correlations according to growth patterns, especially in small samples, could account for some of the previous divergence in the published results.

For all measures of lung function evaluated, correlations in like-sex sibships were always higher than those observed for opposite-sex sibships, which further supports the influence of the growth phenomena on the pattern of observed correlations. The observation that there was a distinct trend toward a decrease in the magnitude of the correlations for FEF_{25-75} and FEF_{25-75}/FVC from male-sex sibships to opposite-sex sibships would be expected on the basis of the growth data in figures 1–3. This explanation cannot easily be invoked to account for the pattern of correlations for FVC. However, in the case of FEV_1, the near identity between same-sex sibships would be expected, as would a decrease in magnitude for opposite-sex sibships. The results may also explain, in part, the small correlations in opposite-sex sibships observed by Higgins and Keller (1) and Devor and Crawford (23), although in the former study subjects were generally older than in the present work (age data are not given in the study by Devor and Crawford). The pattern of correlations between 5.5 and 40 years of age according to the data of the PAARC and Tecumseh studies suggests that maternal factors, prenatal or postnatal, have a substantial effect on the phenotypic expression of lung function for girls and boys through the mid-teenage years. During the teens, the sex-specific environment of children, partly derived from their parents, exerts increasing effects. By adulthood, children do not generally share a common environment with their parents, in which case, the influence of their personal environment increases the variability of lung function and thus reduces the apparent magnitude of the familial effect (1).

Investigation of parental smoking habits revealed that age-, height-, town-, and, where appropriate, weight-adjusted levels of lung function in children were significantly lower in children with mothers who smoked (table 3). No effect was seen for paternal smoking. These results are consistent with other reported data (18, 24–27). Furthermore, since French mothers who smoke generally belong to a higher educational group and French fathers who smoke to a lower educational group (11), the effect of maternal smoking as well as the lack of association with paternal smoking are unlikely due to social class confounders. Recently, a significant effect of paternal smoking on children's lung function values was reported, but these children were older (8–16 years) and lived in crowded homes (28).

As expected, mothers who smoked had a lower body mass index. Therefore, adjustment for maternal ponderal index may lead to an underestimate of the effect of maternal smoking. Furthermore, if a low body mass index relates to a susceptibility among smokers (possibly genetically controlled) to lower lung function (29, 30), adjustment for maternal body mass index may lead to an underestimate of resemblance (in terms of lung function) between mothers and children. In the present study, associations between children's lung function and maternal smoking persisted after taking into account the nonindependence of siblings, which confirmed and extended the results of Burchfiel et al. in Tecumseh (31).

A greater time spent by the mother with the young child is a possible explanation of the effect observed with maternal smoking (26, 27). Supporting this hypothesis is the stronger influence of mother's smoking than of father's smoking on children's salivary cotinine (32). Maternal smoking during pregnancy also may have some effect on lung development that carries over into early childhood. This would be consistent with the growth-retarding effect on fetus rats in relation to maternal smoking (33) and to the effect of maternal smoking on height (34). No direct estimate of maternal smoking during pregnancy was available in this study, nor were enough mothers ex-smokers to evaluate this point indirectly.

For most of the children, the mother was present when the spirometric exam was performed, but this does not explain the higher correlations observed with the mothers because the same pattern was observed when the father was present (4). The proximity of the mother, indirectly assessed by her working status (never, past, current) suggests that, independent of smoking, correlations for FEF_{25-75} between children and mothers are markedly influenced by proximity and, therefore, by postnatal factors. An alternative explanation of this finding might be the existence of important factors modifying maternal

FEF_{25-75} among working mothers, but no significant association has been observed in the PAARC population between occupational exposures and FEF_{25-75} among women (35).

In conclusion, the results suggest that growth patterns and their particular characteristics for each sex appear to be critical factors in the study of familial resemblance of lung function.

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A Critical Analysis of the Relationship Between Parental Smoking and Pulmonary Performance in Children

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Kritische Analyse des Zusammenhangs zwischen den Rauchgewohnheiten der Eltern und der Lungenfunktion der Kinder

Bis heute sind mindestens 24 Arbeiten über epidemiologische Studien erschienen, in denen die Wirkung derzeitiger oder lebenslanger Rauchgewohnheiten der Eltern auf die Lungenfunktionsparameter ihrer Kinder untersucht wird. In diesen Studien, die sich alle im Ansatz ähneln, wurden die Daten über die elterlichen Rauchgewohnheiten und weitere Angaben, die mit Hilfe standardisierter Fragebogen ermittelt worden waren, mit spirometrischen Messungen bei den Kindern statistisch verglichen unter Berücksichtigung des Raucherstatus der Eltern. Eine Übersicht über diese Arbeiten zeigt eine Anzahl von Widersprüchen bezüglich des Zusammenhangs zwischen dem Raucherstatus der Eltern und den Lungenfunktionsparametern der Kinder (FEV_1 oder $FEV_{0.75}$, FEF_{25-75}, FVC und $V_{max\,50\%}$).

Bei der Interpretation der Ergebnisse sollten eine Anzahl Faktoren in Erwägung gezogen werden, insbesondere im Hinblick auf die festgestellten Widersprüche sowie in Anbetracht der Tatsache, daß die Kinder ausschließlich nach den durch Fragebogen ermittelten Daten eingestuft wurden. Dazu gehören das Mißklassifikationsbias, wodurch die Wirkung des elterlichen Rauchens entweder unter- oder überbewertet wird, der sozioökonomische Status, weitere Variablen sowie genetische Faktoren. Ferner müssen die Wirkung des Rauchens während der Schwangerschaft und der Stillzeit und die Tabakrauchexposition des Kindes als mögliche Ursachen einer meßbaren Verminderung der Lungenfunktion bei Kindern in Erwägung gezogen werden.

Summary

To date, at least 24 epidemiologic research papers, of essentially similar design, have been published on the effects of current or lifetime parental smoking on pulmonary function parameters in children. In these studies, parental smoking and other data obtained from standardized questionnaires and spirometric measurements in children were compared statistically according to the smoking status of the parents. A survey of these reports reveals a number of inconsistencies in the association between parental smoking status and pulmonary function parameters (FEV_1 or $FEV_{0.75}$, FEF_{25-75}, FVC, and $V_{max\,50\%}$) in the child.

A number of factors should be considered when interpreting the results of these studies, particularly in light of the observed inconsistencies and the fact that children were classified solely on the basis of questionnaire data. Among these are sources of misclassification bias, which could either underestimate or overestimate parental smoking effect, socioeconomic status, other variables, and genetic factors. Also, effects of maternal smoking *in utero* or on lactation, as well as exposure of the child to environmental tobacco smoke (ETS), need to be considered as possible causes of any apparent decrement in pulmonary function in children.

Key words:

Parental smoking – Maternal smoking – Passive smoking – Involuntary smoking – Environmental tobacco smoke – ETS – Pulmonary function – Children

Introduction

The Committee on Passive Smoking of the National Research Council, National Academy of Sciences (1986) and the Surgeon General of the United States (1986) recently reviewed evidence suggesting an association between parental smoking and increased incidence of respiratory symptoms and disease in young children. Currently, it is unclear whether this effect is due to environmental tobacco smoke (ETS) exposure or reflects other factors, such as *in utero* effects of maternal smoking or transmission of infection from parents and/or siblings to the child. Effects of parental smoking on volume-flow indices of pulmonary function have also been examined. Such studies in children are of particular interest because developing lungs may be more sensitive to the effects of environmental pollutants, while exposure to ETS may be particularly intense in children, who may spend 60–80% of their time indoors (Binder et al. 1976).

Table 1   Studies of the Effects on Parental Smoking on Pulmonary Function in Normal Children

Published study		Source of subjects	No. subjects (ages)	
1.	Tager et al. 1976	East Boston, Mass.	140	(5–31y)
2.	Tager et al. 1979	East Boston, Mass.	261	(5–19y)
3.	Weiss et al. 1980	East Boston, Mass.	238	(5–10y)
4.	Tager et al. 1983[L]	East Boston, Mass.	715	(4–28y)
5.	O'Connor et al. 1987	East Boston, Mass.	265	(6–21y)
6.	Ware et al. 1984	Six U. S. cities	7.112	(6–9y)
7.	Berkey et al. 1986[L]	Six U. S. cities	7.834	(6–10y)
8.	Hasselblad et al. 1981	Seven U. S. areas	16.689	(6–13y)
9.	Tashkin et al. 1984	Los Angeles, Cal.	971	(7–17y)
10.	Ekwo et al. 1983	Iowa City, Ia.	183	(6–12y)
11.	Veda et al. 1984	Western Pa.	3.175	(5–14y)
12.	Spinaci et al. 1985	Turin, Italy	2.385	(11y[a])
13.	Chen and Li 1986	Shanghai, China	571	(8–16y)
14.	Burchfiel et al. 1986	Tecumseh, Mich.	591	(10–19y)
15.	Yarnell and St. Leger 1979	Cardiff, Wales	214	(7–11y)
16.	Teculesco et al. 1986	Vandouvre, France	92	(10–16y)
17.	Tsimoyianis et al. 1987	Nassau County, N. Y.	193	(12–17y)
18.	Lebowitz et al. 1987[L]	Tucson, Arizona	353	(5.5–25y)
19.	Leeder et al. 1976	London, England	454	(5y)
20.	Schilling et al. 1977	Three U. S. cities	816	(7–18y)
21.	Speizer et al. 1980	Six U. S. cities	5.842	(6–10y)
22.	Dodge 1982[L]	Three Arizona towns	472	(8–10y)
23.	Lebowitz et al. 1984	Tucson, Arizona	271	(13.5y[a])
24.	Lebowitz 1984	Tucson, Arizona	24	(4–24y)

[L] Indicates longitudinal study, otherwise cross-sectional
[a] Average age

Basic Design and Results of Pulmonary Function Studies in Children

To date, at least 24 epidemiologic research papers, of essentially similar design, have been published on the effects of current or life-time parental (or household) smoking on pulmonary function in children (Table 1). In these studies, parental smoking and other data were obtained from standardized questionnaires, usually derived from or similar to the British Medical Research Council questionnaire. Spirometric measurements obtained in the children, usually normalized, were compared statistically according to the smoking status of the parents. Most of these studies have been cross-sectional in nature, although four have been longitudinal, with the particular objective of assessing ETS effects on lung growth and development (studies 4, 7, 18, 22).

Table 2 presents the results of the findings of these studies as they relate to the effects of parental smoking on two commonly used pulmonary function parameters, forced expiratory volume in the first (or 0.75) second (FEV_1 or $FEV_{0.75}$) and forced expiratory flow between the first and last 25% of the forced vital capacity maneuver (FEF_{25-75}). Of 21 studies which measure FEV_1 or $FEV_{0.75}$, 11 report a small ($\leq 7\%$) decrement in this parameter (studies 1, 4–8, 12–16) associated with parental (usually maternal) smoking, while 10 do not (studies 2, 3, 9–11, 18, 20–23). Of the 11 studies measuring FEF_{25-75}, 8 report a decrement in this measurement in children of smoking parents (usually mothers) (studies 2, 3, 5, 9, 11, 13, 15, 17) while 3 do not (studies 4, 10, 12).

In 10 of these studies, the effects of parental smoking on both FEV_1 (or $FEV_{0.75}$) and FEF_{25-75} in children were measured simultaneously (Table 2). A concurrent

Table 2   Effects of Parental Smoking on FEV_1 ($FEV_{0.75}$) and FEF_{25-75} in Normal Children

Study Number[#]	Effects on FEV_1 or $FEV_{0.75}$	Effects on FEF_{25-75}	Comments
1.	decr.[*]	not reported	males only
2.	none	decr.	change not statist. signif.
3.	none	decr.[*]	
4.	decr. 7%[*]	none	decrement in lung growth over 5 years
5.	decr. 5–7%[*]	decr. 14–15%[*]	
6.	decr. 0.6–0.9%[*]	not reported	
7.	decr. 0.85%[*]	not reported	predicted decrement in lung growth over 5 years
8.	decr. 0.5–2.0%[*]	not reported	measured $FEV_{0.75}$
9.	none	decr. 2.5%[*]	effect in females (12–15y) only
10.	none	none	increased responses to isoproterenol
11.	none	decr. 4%[*]	measured $FEV_{0.75}$; females only
12.	decr.	none	data not presented
13.	decr. 3%	decr. 6%	assoc. with paternal smoking
14.	decr. 4–5%	not reported	males only
15.	decr. 3%[*]	decr. 12%[*]	measured $FEV_{0.75}$; females only; no statistical testing performed
16.	decr. 5%	not reported	males only; decr. attributed to taller children in smoking group
17.	not done	decr.[+]	not statistically significant; based on increased incidence of children with FEF_{25-75} less than 70% predicted value
18.	none	not done	suggested effect on $V_{max\ 50\%}/FVC$[*]
19.	not done	not done	measured peak flows
20.	none	not reported	
21.	none	not reported	
22.	none	not reported	measured yearly lung growth rates
23.	none	not reported	
24.	not done	not done	measured peak flows[+]

[#] Numbers correspond to those in Table 1.
[*] Associated mainly or exclusively with maternal smoking
[+] Associated with household tobacco use

decrease in both parameters in children of smoking parents was reported in 3 studies (5, 13, 15). Two studies reported a decrease in FEV_1 without a decrease in FEF_{25-75} (4 and 12), 4 studies reported the converse situation (2, 3, 9, 11), and 1 study (10) reported no effect on either parameter.

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Table 3   "Dose"-Related Effects of Parental Smoking on Pulmonary Function in Normal Children

Study Number[*]	Parameter	Varies with the no. of Cigarettes	Varies with the no. of Smokers
1.	FEV_1	yes	not avail.
4.	FEV_1	not done	no
6.	FEV_1	yes	no/yes[c]
7.	FEV_1	yes	yes[d]
8.	$FEV_{0.75}$	yes	no
13.	FEV_1	yes	yes
14.	FEV_1	yes[a,b]	yes[a,b]
15.	$FEV_{0.75}$	no	not avail.
2.	FEF_{25-75}	not done	yes[a]
3.	FEF_{25-75}	not done	yes
9.	FEF_{25-75}	no	not avail.
11.	FEF_{25-75}	no	no
13.	FEF_{25-75}	yes	yes
15.	FEF_{25-75}	yes	not avail.

[*]   Numbers correspond to those in Table 1.
[a]   Concluded on the basis of trends
[b]   Males only
[c]   In 1 of 2 examinations effect was proportional to number of smokers.
[d]   Proportional to number of smokers for FEV level, not for pulmonary growth rate

Table 4   Effects of Parental Smoking on FVC, PEFR, and V_{max} 50% in Normal Children

Study Number[*]	FVC	PEFR	V_{max} 50%
5.	none		
6.	incr.		
7.	none		
9.	none		decr.[c]
10.	none	none	none
11.	incr.		
12.	none		none
14.	decr.[a]		decr.[b]
15.	none		
16.	none		decr.[a]
17.	none		
18.	incr.		none
19.		none	
20.	none	none	decr.[b]
21.	incr.		
23.	none		none
24.		none	

[*]   Numbers correspond to those in Table 1.
[a]   Males only
[b]   Females only
[c]   Males, 7–11y; females, 12–17y

A number of the papers report the results of studies done at different times on the same population of children (studies 1–5 and studies 6, 7, 21), and reveal inconsistent effects on both parameters, examined either separately or concurrently. Three studies lack statistical verification of the significance of the effects observed (studies 2, 15, 17). In some of the studies, effects are noted in one gender of child and not the other (studies 1, 9, 11, 14–16). In two reports, there were no apparent effects on FEV_1, or FEF_{25-75}, but effects on other pulmonary function parameters were noted (studies 10, 18).

Table 3 presents the reported dose-response relationships between these pulmonary function parameters in children and quantitative estimates of tobacco smoke exposure. FEV_1 (or $FEV_{0.75}$) varied inversely with the number of cigarettes smoked by the parent in six of seven studies (1, 6, 7, 8, 13, 14, 15) and with the number of household smokers in four of six studies (4, 6, 7, 8, 13, 14). FEF_{25-75} varied inversely with number of cigarettes smoked in two of four studies (9, 11, 13, 15) and with the number of household smokers in three of four studies (2, 3, 11, 13). An inverse dose-related effect associated with the number of cigarettes smoked was usually, but not always, accompanied by an effect associated with the number of smokers, where both types of observation were made.

Other pulmonary function parameters in children have also been examined with respect to effects of parental smoking in some of the studies (Table 4). Of the 15 studies which present data on forced vital capacity (FVC), parental smoking is associated with an increase in this parameter in four (6, 11, 18, 21), a decrease in this parameter in males in one (14), and no change in the remaining studies (5, 7, 9, 10, 12, 15–17, 20, 23). No association between peak expiratory flow rate (PEFR) in children and parental smoking was found in the four reports which have measured this parameter (studies 10, 19, 20, 24). When other parameters have been

measured, the findings from one study to the next have either been inconsistent, as in the case of V_{max} 50% (Table 4), or have been insufficiently replicated to assess the degree of consistency.

A small number of studies have examined the effect of parental or household smoking on pulmonary function in asthmatic children. Three studies report no apparent effect of parental or household smoking on baseline pulmonary parameters, such as FEV_1, FEF_{25-75}, or PEFR, in asthmatic children (*Tashkin* et al. 1984 [study 9]; *Evans* et al. 1987; *O'Connor* et al. 1987 [study 5]). On the other hand, *Murray* and *Morrison* (1986) report that maternal smoking is associated with a 13% decrease in FEV_1 and a 23% decrease in FEF_{25-75} in asthmatic children. In addition, these investigators observed a fourfold increase in the bronchoconstrictor response to histamine in asthmatic children with smoking mothers. Similarly, *O'Connor* et al. (1987) (study 5) suggest a hyperresponsiveness (ie., increased bronchoconstriction) in asthmatic children of smoking parents to cold air bronchial challenge although, as stated above, no decrement in baseline function was observed in this group. *Ekwo* et al. (study 10) reported increased bronchodilatation in response to isoproterenol in nonasthmatic children of smoking mothers. The significance of these various observations regarding bronchial responsiveness remains to be determined.

Factors Influencing the Outcome of Studies Relating Parental Smoking to Pulmonary Function in Children

The majority of the 24 studies reviewed above (1–18) conclude that parental (usually maternal) smoking produces decrements in pulmonary function in children. However, as pointed out in the preceding section, inconsistencies exist in the specific parameters examined, both between different sample populations and within the same sample population. In the absence of biologic markers (*Jarvis* et al.

, 1985) or some other method of verification, the validity of the questionnaire exposure data in these studies remains to be determined and is, at least, open to some uncertainty. In addition, several factors can influence the results of such studies either "positively" or "negatively", and hence, may contribute to some of the inconsistencies observed in the data. Among these factors are misclassification bias, socioeconomic status, and other variables.

Misclassification Bias

Misclassification errors in the assignment of subjects to groups can create bias that either diminishes or exaggerates effects. One source of misclassification bias is erroneous reporting of parental smoking status. It has recently been estimated that as many as 5 per cent of the respondents in epidemiologic studies who claim to be never smokers are either current or ex-smokers (Committee on Passive Smoking, 1986). Under these circumstances, a child of a misclassified smoker or ex-smoker will be incorrectly classified into the non-smoking or never smoking parents group, thereby leading to an underestimation of parental smoking-related effects. Similar misclassification bias can result from a change of parental smoking status. It has been reported that smoking status may change at a rate of 1.25 to 2.5 % per year (Berkey et al. 1986 [study 7]). In studies where subjects are classified on the basis of *current* parental smoking (studies 4–12, 14, 15, 18, 20, 22) rather than lifetime exposure (studies 1, 2, 13, 19, 23), this would also result in the unexposed group containing misclassified exposed children, which would also tend to underestimate parental smoking-related effects. Over an extended period of time, the amount of misclassification error due to change of parental smoking status could be substantial (e. g., as high as 15 % in a study of 6 years in duration).

Another source of misclassification bias is lack of consideration or underestimation of active smoking in children. Kerigan et al. (1986) recently estimated that 24 % of the children between the ages of 8–13 years in a cohort in Hamilton, Ontario reported a history of smoking. A progressive increase in smoking occurred with age, such that at 13 years of age 50 % of the children had smoked, with a significant proportion having smoked in the preceding 4 weeks. Other studies estimate tobacco use by children ranging from 2 % or less (studies 6, 7, 11–14, 23) to up to 26 % (studies 1–3, 5, 9, 17). It has been noted that childhood smoking impairs pulmonary performance (Tager et al. 1979 [study 2]; Lebowitz et al. 1987 [study 18]). If, as has been implied, there is a greater likelihood that smoking parents will have smoking children (Committee on Passive Smoking, 1986; U.S. Surgeon General, 1986; Lebowitz et al. 1987 [study 18]; O'Connor et al. 1987 [study 5]), then this form of misclassification would lead to an overestimation of parental smoking effect.

Treatment of active smoking in children varied among the 24 epidemiologic studies reviewed herein. Although some of the studies obtained estimates of childhood active smoking, usually by questioning children in the absence of their parents (studies 1–7, 9, 11–14, 16–17, 20, 23), it was generally assumed, without specific verification, that children below a certain age were nonsmokers. Depending on the particular study, this age ranged from 9 years (studies 6, 7, 11) to up to 15 years (studies 9, 14, 23). In some studies smoking

children were excluded from the data base (studies 2, 4, 5, 7, 9, 11, 13, 14, 16–18, 20, 23), while in others they were not (studies 1, 3, 6, 8, 10, 15, 19, 21, 22). In one study, the authors suggested that active smoking in children could account for the apparent effect of maternal smoking on pulmonary function in girls aged 12–17 years (Tashkin et al. 1984 [study 9]).

Socioeconomic Status (SES)

It has been shown that the prevalence of parental smoking is inversely related to family income and positively correlated with a number of SES-related factors that potentially can adversely influence childhood pulmonary function, such as poorer outdoor air quality, increased parental coughing, higher gas stove usage, frequent change of address, and lower per capita living space (Kerigan et al. 1986). Furthermore, pulmonary test performance in children appears to be influenced by SES, learning, and motivation (Berkey et al. 1986 [study 7]; Dockery et al. 1983; Kerigan et al. 1986; Ware et al. 1984 [study 6]). Conceivably, active smoking in children, a source of bias discussed above, may also be inversely related to SES.

Appropriate correction for SES is a matter of debate but appears complex. Among the factors proposed by Green (1970) as components of an SES adjustment of a data base in health-related studies are education, income, occupation and ethnicity. In addition, he has suggested that maternal education is more important than paternal education. Some of the studies reviewed here included adjustments for SES (studies 1–4, 6–8, 11–14, 19–21, 23), but others did not (studies 5, 9, 10, 15–17, 22). However, even where adjustments for SES were made, the procedures were not as rigorous as those proposed by Green. For example, one method of correction for SES was based on the average educational attainment of both parents (less than high school, high school, more than high school) (studies 6 and 7). Such an adjustment cannot discriminate between a household in which both parents have achieved a modest level of education and one in which one parent was highly educated and the other was not. Furthermore, it may be extremely difficult, solely on the basis of relatively crude estimates of SES, to adjust for SES-related factors that may influence respiratory performance and health, such as family attitudes and practices with regard to nutrition, exercise, and stress management.

Other Factors

Although statistical significance is generally assumed to reflect a real or treatment effect and the statistical methodology is presumed to minimize the possibility of chance effects, statistically significant differences can still be due to uncontrolled factors (biases) and/or chance variation (Inglefinger et al. 1983). It has been shown that mean pulmonary performance within a single group of children can vary significantly from one spirometry test to the next (Kerigan et al. 1986) without any apparent cause. It is noteworthy that such statistically significant differences are similar in magnitude to most of the small decrements in pulmonary function (generally $\leq$ 5 %) reported in children of smoking parents.

Among the other factors which could have influenced the outcome of the above epidemiologic studies are outdoor air quality, home heating, air conditioning and humidity, and occupational exposures (which can be a factor in older children). These may or may not be related to SES. Several studies have noted familial aggregation of pulmonary performance (Tager et al. 1976 [study 1]; Lebowitz et al. 1984 [study 23]; Higgins and Keller, 1975; and Lewitter et al. 1984) suggestive of a genetic relationship. Lebowitz et al. (1984 [study 23]) found that adjustment for a genetic variable, body habitus, eliminated any apparent association between maternal smoking and pulmonary performance in children when comparisons were made on the basis of parent-child pairs.

Another issue relates to the mechanism(s) responsible for an effect of maternal smoking on pulmonary function in children. Attribution of such an effect to ambient ETS is presumptive and should not preclude other important considerations. For example, it has been reported that smoking during pregnancy adversely affects growth and development of offspring (Abel, 1980) and that maternal smoking may influence lactation (Nyboe-Andersen et al. 1982). Therefore, the possibility that effects of maternal smoking on a child's pulmonary function are mediated by in utero or lactational mechanisms should also be considered. The findings of two studies are consistent with this possibility (Stern et al. 1987; Yarnell and St. Leger, 1979 [study 15]).

The dose-response relationship between some pulmonary function parameters in children and amount of parental smoking and/or number of smokers in the household is an extremely important criterion and requires further examination. Although the available dose-response data are consistent with an effect of ETS, they are also consistent with the alternative possibilities of childhood smoking, socioeconomic status, and in utero and/or lactational mechanisms. Smoking among children may be more likely to occur where parents are heavier smokers and/or where there are more smokers in the household. Socioeconomic factors affecting pulmonary function may relate quantitatively as well as qualitatively to parental smoking. It is also probable that mothers who smoke more postnatally smoked more during pregnancy and lactation.

Summary and Conclusions

There are a number of factors that must be considered in evaluating the published studies dealing with parental smoking and pulmonary function in children, especially in light of the various inconsistencies noted here in the reported data. These include sources of misclassification bias, socioeconomic status and other variables, and genetic factors. Consideration must also be given to in utero and lactational mechanisms, in addition to ambient ETS, as possible explanations of the findings.

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Buchbesprechungen

Ebel, S., J. Roth (Hrsg.): Lexikon der Pharmazie. Studienausgabe. Bearbeitet von 17 Autoren. 1987. X, 704 S., 2177 Formeldarstellungen und Abb. (Georg Thieme Verlag Stuttgart · New York.) Kart. DM 88,–. ISBN: 3 13 715201 1

Wenige Monate nach dem Erscheinen des Lexikons der Pharmazie von Ebel und Roth liegt nun auch eine Studienausgabe des Werkes in kartoniertem Einband vor. Der Kaufpreis konnte dadurch immerhin um 40,– DM gesenkt werden, was die Verbreitung des Nachschlagewerkes insbesondere in den weniger zahlungskräftigen Studentenkreisen mit Sicherheit fördern wird.

Bereits bei der Besprechung der gebundenen Ausgabe wies der Rezensent auf die hohe fachliche Qualität des Lexikons hin, die durch die Mitwirkung von 17 bekannten Vertretern der verschiedenen pharmazeutischen Spezialgebiete verkörpert wird. Die

Autoren der Stichworte sind zum großen Teil Hochschullehrer der pharmazeutischen Biologie, Chemie und Technologie sowie der Pharmaziegeschichte, stammen aber auch aus dem Bereich der pharmazeutischen Industrie, der Verwaltung und der Verbände.

Hervorzuheben sind neben den Textbeiträgen die vielen graphischen Darstellungen und die Formelbilder für einen Großteil der im Lexikon aufgeführten Substanzen. Das Lexikon der Pharmazie, ein Spiegelbild eines äußerst breit gefächerten Wissensgebietes, kann neben dem Studenten der Pharmazie auch dem praktisch tätigen Apotheker in Offizin, Krankenhaus und Industrie sowie dem in Wissenschaft und Forschung arbeitenden Pharmazeuten, Pharmakologen und Toxikologen empfohlen werden.

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